DECLARATION

I, Yukiharu IWAYA, hereby certify that I am the translator of the certified official copy of the documents in respect of Japanese patent application No.2004-017725 filed on 26 January 2004 and that the following is a true and correct translation to the best of my knowledge and belief.

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12 July 2010

JAPAN PATENT OFFICE

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Applicant(s) : TAKASAGO INTERNATIONAL CORPORATION

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Hiroshi OGAWA
Commissioner,
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[Document Name] SPECIFICATION

[Title of the Invention] PROCESS FOR PRODUCTION OF AMINES

[Technical Field]

[0001]

The present invention relates to a process for the production of amines useful as intermediate or the like for drugs, agricultural chemicals or the like.

[Background Art]

[0002]

For a process for production of an optically active intermediate used for drugs, agricultural chemicals or the like, for example, methods using a metal compound have previously been known. However, the method has a problem that the metal compound used must be disposed of.

[0003]

In order to solve such problem, Non-patent Literature 1 and Non-patent Literature 2 report a method of reacting a carbonyl compound and an imine using L-proline or a derivative thereof in place of a metal compound.

However, the method described in the Non-patent Literature 1 has a problem that after the reaction using L-proline, reduction reaction with a reducing agent such as sodium borohydride and the like must be performed, and the method described in the Non-patent Literature 2 has a problem that a large amount (more than a catalytic amount) of the catalyst of L-proline must be used.

[0004]

Non-patent Literature 3 describes a process for production of an optically active N-protected β-amino acid by reacting

trimethylsilyl vinyl ether and an N-(2-hydroxyphenyl)imine with a chiral phosphoric acid derivative.

However, the method described in the Non-patent Literature 3 has a problem that a substrate to be reacted with an imine must be trimethylsilylated into polymethylsilyl vinyl ether.

[0005]

[Non-patent Literature 1] J. Org. Chem., Vol. 68, No. 25, 9624 (2003).

[Non-patent Literature 2] J. Am. Chem. Soc., Vol. 24, No. 9, 1842 (2002).

[Non-patent Literature 3] THE NINTH INTERNATIONAL KYOTO CONFERENCE OF NEW ASPECTS OF ORGANIC CHEMISTRY, Program, Abstracts, List of Participants, p116, (2003).

[Disclosure of the Invention]

[Problems to be Solved by the Invention]

[0006]

The present invention was done in view of the aforementioned problems, and an object of the present invention is to provide a process of production of amines useful as an intermediate or the like for drugs, agricultural chemicals or the like, particularly, optically active amines in a good yield and a high optical purity without extra post-treatment or the like, and a phosphoric acid derivative, particularly, an optically active phosphoric acid derivative useful for production of the amines or the like.

[Means to Solve the Problems]

[0007]

In order to solve the aforementioned problems, the present inventors have intensively studied and, as a result, have found

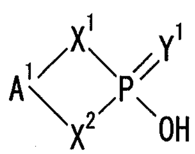
that desired amines are obtained in a good yield and a high optical purity by using a phosphoric acid derivative represented by the general formula (1), thereby to complete the present invention.

[0008]

That is, the present invention is as follows:

1) a process for preparing an amine, comprising reacting an imine compound and a nucleophilic compound (provided that trialkylsilyl vinyl ethers are excluded) in the presence of a phosphoric acid derivative represented by the general formula (1):

[0009]



(1)

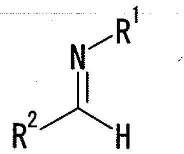
[0010]

(wherein A^1 represents a spacer; X^1 and X^2 each independently represent a divalent nonmetal atom or a divalent nonmetal atomic group; and Y^1 represents an oxygen atom or a sulfur atom);

2) the process according to the above 1), wherein the phosphoric acid derivative represented by the general formula (1) is an optically active phosphoric acid derivative, and the obtained amine is an optically active amines;

3) the process according to the above 1), wherein the imine compound is an imine compound represented by the general formula (2):

[0011]

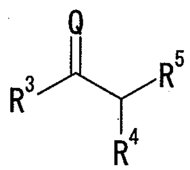
 (2)

[0012]

(wherein R^1 represents a hydrogen atom or a protecting group, and R^2 represents a group having no α-proton or represents an unsaturated hydrocarbon group);

4) the process according to the above 1), wherein the nucleophilic compound is a compound represented by the general formula (3):

[0013]

 (3)

[0014]

(wherein R^3 represents a hydrogen atom, a hydrocarbon group optionally having a substituent, a heterocyclic group optionally having a substituent, an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent, an aralkyloxy group optionally having a substituent or a substituted amino group;

R^4 and R^5 each independently represent a hydrogen atom, a hydrocarbon group optionally having a substituent, a heterocyclic group optionally having a substituent, EWG^1 (EWG^1 represents an electron withdrawing group), an alkoxy group optionally having a substituent, an aryloxy group optionaly having a substituent, an aralkyloxy group optionally having a substituent, an alkylthio group optionally having a substituent, an arylthio group optionally having a substituent, an

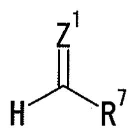
aralkylthio group optionally having a substituent or a hydroxy group;

Q represents a group giving a tautomer of a compound represented by the general formula (3); or

R^3 and R^4, R^3 and R^5, or R^4 and R^5 may be taken together to form a ring);

a compound represented by the general formula (5):

[0015]



(5)

[0016]

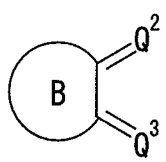
(wherein R^7 represents a hydrogen atom, a hydrocarbon group optionally having a substituent, a heterocyclic group optionally having a substituent, an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent or an aralkyloxy group optionally having a substituent, an alkylthio group optionally having a substituent, an arylthio group optionally having a substituent, an aralkylthio group optionally having a substituent or EWG^2 (EWG^2 represents an electron withdrawing group), and

Z^1 represents N_2, $P(R^8)_3$ (three R^8s are the same or different, and each represent a hydrogen atom, a hydrocarbon group optionally having a substituent, a heterocyclic group optionally having a substituent, an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent or an aralkyloxy group optionally having a substituent) or CR^9R^{10} (R^9 and R^{10} each independently represent a hydrogen atom, a hydrocarbon group optionally having a substituent, a heterocyclic group optionally having a

substituent, an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent, an aralkyloxy group optionally having a substituent, an alkylthio group optionally having a substituent, an arylthio group optionally having a substituent, an aralkylthio group optionally having a substituent, an amino group or a substituted amino group, provided that either one of R^9 and R^{10} represents an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent, an aralkyloxy group optionally having a substituent, an alkylthio group optionally having a substituent, an arylthio group optionally having a substituent, an aralkylthio group optionally having a substituent, an amino group or a substituted amino group); or

a compound represented by the general formula (7):

[0017]



(7)

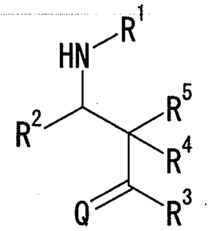
[0018]

(wherein ring B represents an aliphatic ring or an aliphatic heterocycle, and Q^2 and Q^3 each independently represent an oxygen atom, NR^{17} (R^{17} represents a hydrogen atom or a protecting group) or a sulfur atom);

5) the process according to the above 1), wherein the obtained amine is

an amine represented by general formula (4):

[0019]



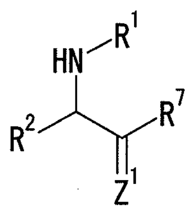
(4)

[0020]

(wherein R^1 to R^5 and Q are the same as defined above);

an amine represented by the general formula (6):

[0021]



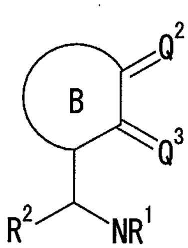
(6)

[0022]

(wherein R^1, R^2, R^7 and Z^1 are the same as defined above); or

an amine represented by the general formula (8):

[0023]



(8)

[0024]

(wherein R^1, R^2, Q^2 and Q^3 are the same as defined above);

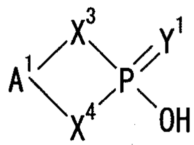
6) the process according to the above 5), wherein the amine represented by the general formula (4), (6), or (8) is an optically active amine;

7) the process according to the above 1), wherein the divalent nonmetal atom or the divalent nonmetal atomic group represented by X^1 and X^2 in the general formula (1) is an oxygen atom, $-NR^{13}-$

(R^{13} represents a hydrogen atom, a hydrocarbon group optionally having a substituent or an acyl group optionally having a substituent), a sulfur atom or $-CR^{15}R^{16}-$ {R^{15} and R^{16} each independently represent a hydrogen atom, a hydrocarbon group optionally having a substituent or EWG^3 (EWG^3 represents an electron withdrawing group), provided that either one of R^{15} and R^{16} is EWG^3};

8) a phosphoric acid derivative represented by the general formula (1a):

[0025]



(1a)

[0026]

(wherein A^1 represents a spacer; X^3 and X^4 each independently represent an oxygen atom, $-NR^{13}-$ (R^{13} represents a hydrogen atom, a hydrocarbon group optionally having a substituent or an acyl group optionally having a substituent), a sulfur atom or $-CR^{15}R^{16}$ {R^{15} and R^{16} each independently represent a hydrogen atom, a hydrocarbon group optionally having a substituent or EWG^3 (EWG^3 represents an electron withdrawing group), provided that either one of R^{15} and R^{16} is EWG^3}; and

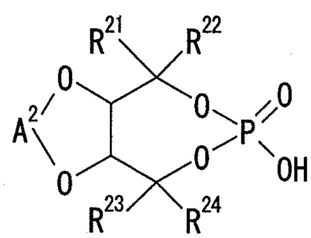
Y^1 represents an oxygen atom or a sulfur atom, provided that when i) $X^3=X^4$, then X^3 and X^4 are each $-NR^{13}-$ (R^{13} is a hydrogen atom, a hydrocarbon group optionally having a substiuent or an acyl group optionally having a substituent), a sulfur atom or $-CR^{15}R^{16}-$, or when X^3 and X^4 are each $-NR^{13}-$, then the $-NR^{13}-$ is $-NR^a-$ (R^a represents an acyl group derived from sulfonic acid), or when ii) X^3 and X^4 are different from each other, then either one of X^3 and X^4 is $-NR^{13}-$, and the $-NR^{13}-$ is $-NR^a-$ (R^a represents

an acyl group derived from sulfonic acid) and the other is an oxygen atom, $-NR^{13}-$ (R^{13} represents a hydrogen atom, a hydrocarbon group optionally having a substituent or an acyl group optionally having a substituent), a sulfur atom or $-CR^{15}R^{16}-$);

9) the phosphoric acid derivative according to the above 8), wherein the phosphoric acid derivative represented by the general formula (1a) is an optically active phosphoric acid derivative;

10) the phosphoric acid derivative represented by the general formula (1b):

[0027]



(1b)

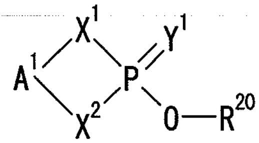
[0028]

(wherein A^2 represents a spacer, and R^{21} to R^{24} each independently represent a hydrocarbon group optionally having a substituent or a hetrocyclic group optionally having a substituent);

11) the phosphoric acid derivative according to the above 10), wherein the phosphoric acid derivative represented by the general formula (1b) is an optically active phosphoric acid derivative;

12) a phosphoric acid derivative represented by the general formula (9):

[0029]



(9)

[0030]

(wherein A^1 represents a spacer; X^1 and X^2 each independently represent a divalent nonmetal atom or a divalent nonmetal atomic group; Y^1 represents an oxygen atom or a sulfur atom; and R^{20} represents an allyl group optionally having a substituent or a benzyl group optionally having a substituent).

[Effect of the Invention]

[0031]

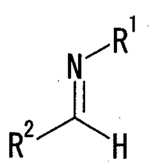
The process of the present invention exerts the effect that since the process uses a phosphoric acid derivative represented by the general formula (1) having no metal atom in the molecule as a catalyst, any extra post-treatment is not necessary, therefore, workability is considerably improved.

[Best Mode for Carrying Out the Invention]

[0032]

Examples of the imine compound used in the present invention include an imine compound represented by the general formula (2):

[0033]



(2)

[0034]

(wherein R^1 represents a hydrogen atom or a protecting group, and R^2 represents a group having no α-proton or represents an unsaturated hydrocarbon group.)

[0035]

In the general formula (2), as a protecting group represented by R^1, any protecting group can be used as far as it is used as an amino protecting group, and examples of such protecting groups include those described as an amino protecting group in "PROTECTIVE GROUPS IN ORGANIC SYNTHESIS THIRD EDITION (JOHN WILEY & SONS,INC. (1999)". Examples of the protecting group (amino protecting group) represented by R^1 include a hydrocarbon group optionally having a substituent, a heterocyclic group optionally having a substituent, an acyl group optionally having a substituent, an alkoxycarbonyl group optionally having a substituent, an aryloxycarbonyl group optionally having a substituent, an aralkyloxycarbonyl group optionally having a substituent, an amimosulfonyl group, an alkoxysulfonyl group and the like.

[0036]

Examples of the hydrocarbon group optionally having a substituent include a hydrocarbon group and a substituted hydrocarbon group. Examples of the hydrocarbon group include an alkyl group, an alkenyl group, an alkynyl group, an alkadienyl group, an aryl group, an aralkyl group and the like.

The alkyl group may be straight-chain, branched, or cyclic alkyl group having 1 to 20 carbon atom(s), and examples of such alkyl group include methyl, ethyl, n-propyl, 2-propyl, n-butyl, 2-butyl, isobutyl, tert-butyl, n-pentyl, 2-pentyl, tert-pentyl, 2-methylbutyl, 3-methylbutyl, 2,2-dimethylpropyl, n-hexyl, 2-hexyl, 3-hexyl, tert-hexyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 2-methylpentan-3-yl, heptyl, octyl, nonyl, decyl, lauryl,

stearyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and the like. Inter alia, the alkyl group is preferably an alkyl group having 1 to 15 carbon atom(s), more preferably an alkyl group having 1 to 10 carbon atom(s).

The alkenyl group may be straight-chain or branched alkenyl group having 2 to 20 carbon atoms, and examples of such alkenyl group include ethenyl, propenyl, 1-butenyl, pentenyl, hexenyl, heptenyl, octenyl, nonenyl, decenyl and the like. Inter alia, the alkenyl group is preferably an alkenyl group having 2 to 15 carbon atoms, more preferably an alkenyl group having 2 to 10 carbon atoms, further more preferably an alkenyl group of having 2 to 6 carbon atoms.

The alkynyl group may be straight-chain or branched alkynyl group having 2 to 20 carbon atoms, and examples of such alkynyl group include ethynyl, 1-propynyl, 2-propynyl, 1-butynyl, 3-butynyl, pentynyl, hexynyl and the like. Inter alia, the alkynyl group is preferably an alkynyl group having 2 to 15 carbon atoms, more preferably an alkynyl group having 2 to 10 carbon atoms, further more preferably an alkynyl group having 2 to 6 carbon atoms.

The alkadienyl group may be straight-chain, branched, or cyclic alkadienyl group having 4 or more carbon atoms, preferably 4 to 20 carbon atoms, containing two double bonds in the chain of the aforementioned alkyl moiety, and examples of such alkadienyl group include 1,3-butadienyl, 2,4-butadienyl, 2,3-dimethyl-1,3-butadienyl and the like. Inter alia, the alkadienyl group is more preferably an alkadienyl group having 4 to 15 carbon atoms, further more preferably an alkadienyl group having 4 to 10 carbon atoms.

The aryl group may be, for example, an aryl group having 6 to 20 carbon atoms, and examples of such aryl group include phenyl, naphthyl, anthryl, biphenyl and the like. Inter alia, the aryl group is preferably an aryl group having 6 to 15 carbon atoms.

The aralkyl group is, for example, a group in which at least one hydrogen atom of the aforementioned alkyl group is substituted with the aryl group, for example, an aralkyl group having 7 to 20 carbon atoms, and examples of such aralkyl group include benzyl, 2-phenylethyl, 1-phenylpropyl, 3-naphthylpropyl and the like. Inter alia, the aralkyl group is preferably an aralkyl group having 6 to 15 carbon atoms.

[0037]

Examples of the substituted hydrocarbon group (hydrocarbon group having a substituent) include a hydrocarbon group in which at least one hydrogen atom of the aforementioned hydrocarbon group is substituted with a substituent. Examples of the substituted hydrocarbon group include a substituted alkyl group, a substituted alkenyl group, a substituted alkynyl group, a substituted alkadienyl group, a substituted aryl group, a substituted aralkyl group and the like. The substituent will be described later.

[0038]

Examples of the heterocyclic group optionally having a substituent include a heterocyclic group and a substituted heterocyclic group. Examples of the heterocyclic group include an aliphatic heterocyclic group and an aromatic heterocyclic group.

Examples of the aliphatic heterocyclic group include a 5

to 8-membered, preferably 5- or 6-membered monocyclic aliphatic heterocyclic group, and a polycyclic or fused aliphatic heterocyclic group having 2 to 20 carbon atoms, which contains at least one, preferably 1 to 3 heteroatom(s) such as a nitrogen atom, an oxygen atom and/or a sulfur atom as a heteroatom. Examples of the aliphatic heterocyclic group include a pyrrolidyl-2-one group, a piperidino group, a piperazinyl group, a morpholino group, a morpholinyl group, a tetrahydrofuryl group, a tetrahydropyranyl group, a tetrahydrofuranyl group and the like. Inter alia, the aliphatic heterocyclic group is preferably an aliphatic heterocyclic group having 2 to 14 carbon atoms.

The aromatic heterocyclic group is, for example, a 5- to 8-membered, preferably 5- or 6-membered monocyclic heteroaryl group, or a polycyclic or fused cyclic heteroaryl group, having 2 to 20 carbon atoms, which contains at least one, preferably 1 to 3 heteroatoms such as a nitrogen atom, an oxygen atom and/or a sulfur atom as a heteroatom, and examples of such aromatic heterocyclic group include fury, thienyl, pyridyl, pyrimidiny, pyrazyl, pyridazyl, pyrazolyl, imidazolyl, oxazolyl, thiazolyl, benzofuryl, benzothienyl, quinolyl, isoquinolyl, quinoxalyl, phthalazyl, quinazolyl, naphthyridyl, cinnolyl, benzoimidazolyl, benzooxazolyl, benzothiazolyl, acridyl, acridinyl, and the like. Inter alia, the aromatic heterocyclic group is preferably an aromatic heterocyclic group having 2 to 15 carbon atoms.

Examples of the substituted heterocyclic group (heterocyclic group having a substituent) include a heterocyclic group in which at least one hydrogen atom of the

aforementioned heterocyclic group is substituted with a substituent. Examples of the substituted heterocyclic group (heterocyclic group having a substituent) include a substituted aliphatic heterocyclic group and a substituted aromatic heterocyclic group. The substituents will be described later.

[0039]

Examples of the acyl group optionally having a substituent include an acyl group and a substituted acyl group. Examples of the acyl group include an acyl group having 1 to 20 carbon atom(s) derived from an acid such as carboxylic acids, sulfonic acids, sulfinic acids, phosphinic acids, phosphonic acids and the like, which may be straight-chain, branched, or cyclic.

[0040]

Examples of the acyl group derived from carboxylic acid include an acyl group derived from carboxylic acids such as aliphatic carboxylic acids, aromatic carboxylic acids and the like, and is represented by, for example, $-COR^c$ (wherein R^c represents a hydrogen atom, a hydrocarbon group optionally having a substituent or a heterocyclic group optionally having a substituent (the hydrocarbon group optionally having a substituent and the heterocyclic group optionally having a substituent may be the same as respective groups explained as a protecting group in R^1 in the aforementioned general formula (2))). Examples of the acyl group derived from carboxylic acids include formyl, acetyl, propionyl, butyryl, pivaloyl, pentanoyl, hexanoyl, lauroyl, stearoyl, benzoyl, 1-naphthoyl, 2-naphthoyl and the like. Inter alia, the acyl group is preferably an acyl group having 2 to 18 carbon atoms.

[0041]

Examples of the acyl group derived from sulfonic acids include a sulfonyl group. Examples of the sulfonyl group include a substituted sulfonyl group represented by R^d-SO_2-(R^d represents a hydrocarbon group optionally having a substituent or a heterocyclic group optionally having a substituent (the hydrocarbon group optionally having a substituent and the heterocyclic group optionally having a substituent may be the same as respective groups explained as a protecting group in R^1 in the general formula (2))). Examples of the sulfonyl group include methanesulfonyl, trifluoromethanesulfonyl, phenylsulfonyl, p-toluenesulfonyl and the like.

[0042]

Examples of the acyl group derived from sulfinic acids include a sulfinyl group. Examples of the sulfinyl group include a substituted sulfinyl group represented by R^e-SO- (R^e represents a hydrocarbon group optionally having a substituent, a heterocyclic group optionally having a substituent or a substituted amino group (the hydrocarbon group optionally having a substituent and the heterocyclic group optionally having a substituent may be the same as respective groups explained as a protecting group in R^1 in the general formula (2), and the substituted amino group may be the same as each group explained in a substituent in a hydrocarbon group optionally having a substituent explained as a protecting group in R^1 in the general formula (2))). Examples of the sulfinyl group include methanesulfinyl, benzenesulfinyl, and the like.

[0043]

Examples of the acyl group derived from phosphinic acids include a phosphinyl group. Examples of the phosphinyl group

include a substititued phosphinyl group represented by $(R^f)_2$-PO- (two R^fs are the same or different, and represent a hydrocarbon group optionally having a substituent (the hydrocarbon group optionally having a substituent may be the same as the hydrocarbon group optionally having a substituent explained as a protecting group in R^1 in the general formula (2))). Examples of the phosphinyl group include dimethylphosphinyl, diphenylphosphinyl and the like.

[0044]

Examples of the acyl group derived from phosphonic acids include a phosphonyl group. Examples of the phosphonyl group include a substituted phosphonyl group represented by $(R^gO)_2$-PO-(two R^gs are the same or different, and represent a hydrocarbon group optionally having a substituent (the hydrocarbon group optionally having a substituent may be the same as the hydrocarbon group optionally having a substituent explained as a protecting group in R^1 in the general formula (2))). Examples of the phosphonyl group include dimethylphosphonyl, diphenylphosphonyl and the like.

Examples of the substituted acyl group (acyl group having a substituent) include an acyl group in which at least one hydrogen atom of the aforementioned acyl group is substituted with a substituent. The substituents will be described later.

[0045]

Examples of the alkoxycarbonyl group optionally having a substituent include an alkoxycarbonyl group and a substituted alkoxycarbonyl group. The alkoxycarbonyl group is, for example, an alkoxycarbonyl group having 2 to 20 carbon atoms which may be straight-chain, branched, or cyclic, and examples

of the alkoxycarbonyl group include methoxycarbonyl, ethoxycarbonyl, n-propoxycarbonyl, 2-propoxycarbonyl, n-butyloxycarbonyl, tert-butyloxycarbonyl, pentyloxycarbonyl, hexyloxycarbonyl, 2-ethylhexyloxycarbonyl, lauryloxycarbonyl, stearyloxycarbonyl, cyclohexyloxycarbonyl and the like.

Examples of the substituted alkoxycarbonyl group (alkoxycarbonyl group having a substitutent) include an alkoxycarbonyl group in which at least one hydrogen atom of the aforementioned alkoxycarbonyl group is substituted with a substituent. The substituents will be described later. Examples of the substituted alkoxycarbonyl group include a 2,2,2-trichloroethoxycarbonyl group, a 1,1-dimethyl-2,2,2-trichloroethoxycarbonyl group and the like.

[0046]

Examples of the aryloxycarbonyl group optionally having a substituent include an aryloxycarbonyl group and a substituted aryloxycarbonyl group. The aryloxycarbonyl group is, for example, an aryloxycarbonyl group having 7 to 20 carbon atoms, and its specific examples include phenoxycarbonyl, naphthyloxycarbonyl and the like.

Examples of the substituted aryloxycarbonyl group (aryloxycarbonyl group having a substituent) include an aryloxycarbonyl group in which at least one hydrogen atom of the aforementioned aryloxycarbonyl group is substituted with a substituent. The substituents will be described later.

[0047]

Examples of the aralkyloxycarbonyl group optionally having a substituent include an aralkyloxycarbonyl group and a substituted aralkyloxycarbonyl group. Examples of the

aralkyloxycarbonyl group is, for example, an aralkyloxycarbonyl group having 8 to 20 carbon atoms, and its specific examples include benzyloxycarbonyl, phenylethoxycarbonyl, p-fluorenylmethyloxycarbonyl group and the like.

Examples of the substituted aralkyloxycarbonyl group (aralkyloxycarbonyl group having a substituent) include an aralkyloxycarbonyl group in which at least one hydrogen atom of the aforementioned aralkyloxycarbonyl group is substituted with a substituent. The substituents will be described later. Examples of the substituted aralkyloxycarbonyl group include 4-nitrobenzyloxycarbonyl, 4-methoxybenzyloxycarbonyl, 4-methylbenzyloxycarbonyl, 3,4-dimethoxybenzyloxycarbonyl and the like.

[0048]

Examples of the aminosulfonyl group include an aminosulfonyl group represented by R^i-SO_2- (R^i represents an amino group or a substituted amino group). The substituted amino group represented by R^i may be the same as a substituted amino group as a substituent described later. Examples of the aminosulfonyl group include aminosulfonyl, dimethylaminosulfonyl, diethylaminosulfonyl, diphenylaminosulfonyl and the like.

[0049]

Examples of the alkoxysulfonyl group include an alkoxysulfonyl group represented by R^j-SO_2- (R^j represents an alkoxy group optionally having a substituent, an arylxoxy group optionally having a substituent or an aralkyloxy group optionally having a substituent). The alkoxy group optionally

having a substituent, the aryloxy group optionally having a substituent and the aralkyloxy group optionally having a substituent represented by R^j may be the same as an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent and an aralkyloxy group optionally having a substituent as a substituent described later. Examples of the alkoxysulfonyl group include methoxysulfonyl, ethoxysulfonyl, phenoxysulfonyl, benzyloxysulfonyl and the like.

[0050]

Examples of the substituent include a hydrocarbon group optionally having a substituent, a halogen atom, a halogenated hydrocarbon group, a heterocyclic group optionally having a substituent, an alkoxy group optionally having a substiuent, an aryloxy group optionally having a substituent, an aralkyoxy group optionally having a substituent, a heteroaryloxy group optionally having a substituent, an alkylthio group optionally having a substituent, an arylthio group optionally having a substituent, an aralkyothio group optionally having a substituent, a heteroarylthio group optionally having a substituent, an acyl group optionally having a substituent, an acyloxy group optionally having a substituent, an alkoxycarbonyl group optionally having a substituent, an aryloxycarbonyl group optionally having a substituent, an aralkyloxycarbonyl group optionally having a substituent, an alkylenedioxy group optionally having a substituent, a nitro group, an amino group, a substituted amino group, a cyano group, a sulfo group, a substituted silyl group, a hydroxyl group, a carboxy group, an alkoxythiocarbonyl group optionally having

a substituent, an aryloxythiocarbonyl group optionally having a substituent, an aralkyloxythiocarbonyl group optionally having a substituent, an alkylthiocarbonyl group optionally having a substituent, an arylthiocarbonyl group optionally having a substituent, an aralkylthiocarbonyl group optionally having a substituent, a carbamoyl group optionally having a subsitutuent, a substituted phosphino group, an aminosulfonyl group, an alkoxysulfonyl group and the like.

[0051]

The hydrocarbon group optionally having a substituent, the heterocyclic group optionally having a substituent, the acyl group optionally having a substituent, the alkoxycarbonyl group optionally having a substituent, the aryloxycarbonyl group optionally having a substituent, the aralkyloxycarbonyl group optionally having a substituent, the aminosulfonyl group and the alkoxysulfonyl group, as a substituent, may be the same as respective groups explained in the aforementioned protecting group.

[0052]

Examples of the halogen atom as a substituent include a fluorine atom, a chlorine atom, a bromine atom, an iodine atom and the like.

[0053]

Examples of the halogenated hydrocarbon group as a substituent include a group in which at least one hydrogen atom of the aforementioned hydrocarbon group is halogenated (e.g. fluorinated, chlorinated, brominated, iodinated etc.). Examples of the halogenated hydrocarbon include a halogenated alkyl group, a halogenated aryl group, a halogenated aralkyl

group and the like.

The halogenated alkyl group is, for example, a halogenated alkyl group having 1 to 20 carbon atom(s), and its specific examples include chloromethyl, bromomethyl, 2-chloroethyl, 3-bromopropyl, fluoromethyl, fluoroethyl, fluoropropyl, fluorobutyl, fluoropentyl, fluorohexyl, fluoroheptyl, fluorooctyl, fluorononyl, fluorodecyl, difluoromethyl, difluoroethyl, fluorocyclohexyl, trifluoromethyl, 2,2,2-trifluoroethyl, 3,3,3-trifluoropropyl, pentafluoroethyl, 3,3,4,4,4-pentafluorobutyl, pentafluoro-n-propyl, perfluoroisopropyl, perfluoro-n-butyl, perfluoroisobutyl, perfluoro-tert-butyl, perfluoro-sec-butyl, perfluoropentyl, perfluoroisopentyl, perfluoro-tert-pentyl, perfluoro-n-hexyl, perfluoroisohexyl, perfluoroheptyl, perfluorooctyl, perfluorononyl, perfluorodecyl, 2-perfluorooctylethyl, perfluorocyclopropyl, perfluorocyclopentyl, perfluorocyclohexyl and the like. Inter alia, the halogenated alkyl group is preferably a halogenated alkyl group having 1 to 10 carbon atom(s).

The halogenated aryl group is, for example, an aryl group having 6 to 20 carbon atoms, and its specific examples include 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl group, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2-bromophenyl, 3-bromophenyl, 4-bromophenyl, 2-iodophenyl, 3-iodophenyl, 4-iodophenyl, 2-trifluoromethylphenyl, 3-trifluoromethylphenyl, 4-trifluoromethylphenyl, 2-trichloroemthylphenyl, 3-trichloromethylphenyl, 4-trichloromethylphenyl, perfluorophenyl, perfluorophenyl, perfluoronaphlthyl, perfluoroanthryl, perfluorobiphenyl and

the like. Inter alia, the aryl group is preferably a halogenated aryl group having 6 to 15 carbon atoms.

The halogenated aralkyl group is, for example, a group in which at least one hydrogen atom of the aforementioned aralkyl group is substituted with a halogen atom, for example, a halogenated aralkyl group having 7 to 20 carbon atoms, and its specific examples include 2-fluorobenzyl, 3-fluorobenzyl, 4-fluorobenzyl, 2-chlorobenzyl, 3-chlorobenzyl, 4-chlorobenzyl, 4-bromobenzyl, 4-iodobenzyl, 2-trifluoromethylbenzyl, 3-trifluoromethylbenzyl, 4-trifluoromethylbenzyl, 4-trichloromethylbenzyl, perfluorobenzyl and the like. Inter alia, the halogenated aralkyl group is preferably a halogenated aralkyl group having 6 to 15 carbon atoms.

[0054]

Examples of the alkoxy group optionally having a substituent as a substituent include an alkoxy group and a substituted alkoxy group. The alkoxy group is, for example, an alkoxy group having 1 to 20 carbon atom(s), which may be straight-chain, branched, or cyclic, and its specific examples include methoxy, ethoxy, n-propoxy, 2-propoxy, n-butoxy, a 2-butoxy, isobutyloxy, tert-butoxy, n-pentyloxy, 2-methylbutoxy, 3-methylbutoxy, 2,2-dimethylpropyloxy, n-hexyloxy, 2-methylpentyloxy, 3-methylpentyloxy, 4-methylpentyloxy, 5-methylpentyloxy, heptyloxy, octylocy, nonyloxy, decyloxy, cyclohexyloxy and the like. Inter alia, the alkoxy group is preferably an alkoxy group having 1 to 10 carbon atom(s), more preferably an alkoxy group having 1 to 6 carbon atom(s).

Examples of the substituted alkoxy group (alkoxy group having a substituent) include an alkoxy group in which at least one hydrogen atom of the aforementioned alkoxy group is substituted with the aforementioned substituent.

[0055]

Examples of the aryloxy group optionally having a substituent as a substituent include an aryloxy group and a substituted aryloxy group. The aryloxy group is, for example, an aryloxy group having 6 to 20 carbon atoms, and its specific examples include phenyloxy, naphthyloxy, anthryloxy and the like. Inter alia, the aryloxy group is preferably an aryloxy group having 6 to 14 carbon atoms.

Examples of the substituted aryloxy group (aryloxy group having a substituent) include an aryloxy group in which at least one hydrogen atom of the aforementioned aryloxy group is substituted with the substituent.

[0056]

Examples of the aralkyloxy group optionally having a substituent as a substituent include an aralkyloxy group and a substituted aralkyloxy group. The aralkyloxy group is, for example, an aralkyloxy group having 7 to 20 carbon atoms, and its specific examples include benzyloxy, 1-phenylethoxy, 2-phenylethoxy, 1-phenylpropoxy, 2-phenylpropoxy, 3-phenylpropoxy, 1-phenylbutoxy, 2-phenylbutoxy, 3-phenylbutoxy, 4-phenylbutoxy, 1-phenylpentyloxy, 2-phenylpentyloxy, 3-phenylpentyloxy, 4-phenylpentyloxy, 5-phenylpentyloxy, 1-phenylhexyloxy, 2-phenylhexyloxy, 3-phenylhexyloxy, 4-phenylhexyloxy, 5-phenylhexyloxy, 6-phenylhexyoxy and the like. Inter alia, the aralkyloxy group

is preferably an aralkyloxy group having 7 to 12 carbon atoms.

Examples of the substituted aralkyloxy group (aralkyloxy group having a substituent) include an aralkyloxy group in which at least one hydrogen atom of the aforementioned aralklyloxy group is substituted with the aforementioned substituent.

[0057]

Examples of the heteroaryloxy group optionally having a substituent as a substituent include a heteroaryloxy group and a substituted heteroaryloxy group. The heteroaryloxy group is, for example, a heteroaryloxy group having 2 to 20 carbon atoms, preferably 2 to 15 carbon atoms containing at least one, at least 1 to 3 heteroatom(s) such as a nitrogen atom, an oxygen atom, a sulfur atom and the like as a heteroatom, and its specific examples include 2-pyridyloxy, 2-pyrazyloxy, 2-pyrimidyloxy, 2-quinolyloxy and the like.

Examples of the substituted heteroaryloxy group (heteroaryloxy group having a substituent) include a heteroaryloxy group in which at least one hydrogen atom of the aralkyloxy group is substituted with the aforementioned substituent.

[0058]

Examples of the alkylthio group optionally having a substituent as a substituent include an alkylthio group and a substituted alkylthio group. The alkylthio group is, for example, an alkylthio group having 1 to 20 carbon atom(s), which may be straight-chain, branched, or cyclic, and its specific examples include methylthio, ethylthio, n-propylthio, 2-propylthio, n-butylthio, 2-butylthio, isobutylthio, tert-butylthio, pentylthio, hexylthio, cyclohexyl and the like.

Inter alia, the alkylthio group is preferably an alkylthio group having 1 to 10 carbon atom(s), more preferably an alkylthio group having 1 to 6 carbon atom(s).

Examples of the substituted alkylthio group (alkylthio group having a substituent) include an alkylthio group in which at least one hydrogen atom of the aforementioned alkylthio group is substituted with the aforementioned substituent.

[0059]

Examples of the arylthio group optionally having a substituent as a substituent include an arylthio group and a substituted arylthio group. The arylthio group is, for example, an arylthio group having 6 to 20 carbon atoms, and its specific examples include a phenylthio group, a naphthylthio group and the like. Inter alia, the arylthio group is preferably an arylthio group having 6 to 14 carbon atoms.

Examples of the substituted arylthio group (arylthio group having a substituent) include an arylthio group in which at least one hydrogen atom of the aforementioned arylthio group is substituted with the aforementioned substituent.

[0060]

Examples of the aralkylthio group optionally having a substituent as a substituent include an aralkylthio group and a substituted aralkylthio group. The aralkylthio group is, for example, an aralkylthio group having 7 to 20 carbon atoms, and its specific examples include benzylthio, 2-phenethylthio and the like. Inter alia, the aralkylthio group is preferably an aralkylthio group having 7 to 12 carbon atoms.

Examples of the substituted aralkylthio group (aralkylthio group having a substituent) include an aralkylthio group in

which at least one hydrogen atom of the aforementioned aralkylthio group is substituted with the aforementioned substituent.

[0061]

Examples of the heteroarylthio group optionally having a substituent as a substituent include a heteroarylthio group and a substituted heteroarylthio group. Examples of the heteroarylthio group is, for example, a heteroarylthio group having 2 to 20 carbon atoms, preferably 2 to 15 carbon atoms, containing at least one, preferably 1 to 3 heteroatom(s) such as a nitrogen atom, an oxygen atom, a sulfur atom and the like as a heteroatom, and its specific examples include 4-pyridylthio, 2-benzimidazolylthio, 2-benzoxazolylthio, 2-benzthiazolylthio and the like.

Examples of the substituted heteroarylthio group (heteroarylthio group having a substituent) include a heteroarylthio group in which at least one hydrogen atom of the aforementioned heteroarylthio group is substituted with the aforementioned substituent.

[0062]

Examples of the acyloxy group optionally having a substituent as a substituent include an acyloxy group and a substituted acyloxy group. The acyloxy group is, for example, an acyloxy group having 2 to 20 carbon atoms derived from carboxylic acids such as aliphatic carboxylic acids, aromatic carboxylic acids and the like, and examples of the acyloxy group include acetoxy, propionyloxy, butyryloxy, pivaloyloxy, pentanoyloxy, hexanoyloxy, lauroyloxy, stearoyloxy, benzoyloxy and the like. Inter alia, the acyloxy group is

preferably an acyloxy group having 2 to 18 carbon atoms.

Examples of the substituted acyloxy group (acyloxy group having a substituent) include an acyloxy group in which at least one hydrogen atom of the aforementioned acyloxy group is substituted with the aforementioned substituent.

[0063]

Examples of the substituted amino group as a substituent include an amino group in which one or two hydrogen atoms of the amino group are substituted with a substituent such as a protecting group and the like. As a protecting group, any protecting group can be used as far as it is used as an amino-protecting group, and its specific examples include those described as an amino protecting group in "PROTECTIVE GROUPS IN ORGANIC SYNTHESIS THIRD EDITION (JOHN WILEY & SONS, INC. (1999)". Examples of the amino protective group include a hydrocarbon group optionally having a substituent, an acyl group optionally having a substituent, an alkoxycarbonyl group optionally having a substituent, an aryloxycarbonyl group optionally having a substituent, an aralkyloxycarbonyl group optionally having a substituent and the like. The hydrocarbon group optionally having a substituent, the acyl group optionally having a substituent, the alkoxycarbonyl group optionally having a substituent, the aryloxycarbonyl group optionally having a substituent and the aralkyloxycarbonyl group optionally having a substituent may be the same as those explained in the aforementioned protecting group.

[0064]

Examples of the amino group substituted with an alkyl group, that is, an alkyl-substituted amino group include a mono- or

di-alkylamino group such as N-methylamino, N,N-dimethylamino, N,N-diethylamino, N,N-diisopropylamino, N-methyl-N-(2-propyl)amino, N-cyclohexylamino and the like.

Examples of the amino group substituted with an aryl group, that is, an aryl-substituted amino group include a mono- or di-arylamino group such as N-phenylamino, N,N-diphenylamino, N-naphthylamino, N-naphthyl-N-phenylamino and the like.

Examples of the amino group substituted with an aralkyl group, that is, an aralkyl-substituted amino group include a mono- or di-aralkylamino group such as N-benzylamino, N,N-dibenzylamino and the like.

In addition, examples of the aralkyl-substituted amino group include a di-substituted amino group such as N-methyl-N-phenylamino, N-benzyl-N-methylamino and the like.

Examples of the amino group substituted with an acyl group, that is, an acylamino group include formylamino, acetylamino, propionylamino, pivaloylamino, pentanoylamino, hexanoylamino, benzoylamino, $-NHSO_2CH_3$, $-NHSO_2C_6H_5$, $-NHSO_2C_6H_4CH_3$, $-NHSO_2CF_3$, $-NHSO_2N(CH_3)_2$ and the like.

Examples of the amino group substituted with an alkoxycarbonyl group, that is, an alkoxycarbonylamino group includes methoxycarbonylamino, ethoxycabonylamino, n-propoxycarbonylamino, n-butoxycarbonylamino, tert-butoxycarbonylamino, pentyloxycarbonylamino, hexyloxycarbonylamino group and the like.

The amino group substituted with an aryloxycarbonyl group, that is, an aryloxycarbonylamino group is, for example, an amino group in which one hydrogen atom of an amino group is substituted with the aforementioned aryloxycarbonyl group, and its specific

examples include phenoxycarbonylamino, naphthyloxycarbonylamino and the like.

Examples of the amino group substituted with an aralkyloxycarbonyl group, that is, an aralkyloxycarbonylamino group include benzyloxycarbonylamino and the like.

[0065]

The alkylenedioxy group optionally having a substituent as a substituent is, for example, such that the adjacent two hydrogen atoms of an aromatic ring in the aforementioned aryl group or aralkyl group are substituted with an alkylenedioxy group optionally having a substitutent. Examples of the alkylenedioxy group optionally having a substituent include an alkylenedioxy group and a substituted alkylenedioxy group. The alkylenedioxy group is, for example, an alkylenedioxy group having 1 to 3 carbon atom(s), and its specific examples include methylenedioxy, ethylenedioxy, trimethylenedioxy, propylenedioxy and the like.

[0066]

Examples of the substituted silyl group as a substituent include a tri-substituted silyl group in which three hydrogen atoms of a silyl group are substituted with a substituent such as an alkyl group, a substituted alkyl group, an aryl group, a substituted aryl group, an aralkyl group, a substituted aralkyl group, an alkoxy group, a substituted alkoxy group and the like. The alkyl group, the substituted alkyl group, the aryl group, the substituted aryl group, the aralkyl group, the substituted aralkyl group, the alkoxy group, and the substituted alkoxy group may be the same as respective groups explained above. Examples of the substituted silyl group

include trimethylsilyl, triethylsilyl, tri(2-propyl)silyl, tert-butyldimethylsilyl, tert-butylbiphenylsilyl, triphenylsilyl, tert-butylmethoxyphenylsilyl, tert-butoxydiphenylsilyl and the like.

[0067]

Examples of the alkoxythiocarbonyl group optionally having a substituent as a substituent include an alkoxythiocarbonyl group and a substituted alkoxythiocarbonyl group. The alkoxythiocarbonyl group is, for example, an alkoxythiocarbonyl group having 2 to 20 carbon atoms, which may be straight-chain, branched, or cyclic, and its specific examples include methoxythiocarbonyl, ethoxythiocarbonyl, n-propoxythiocarbonyl, 2-propoxythiocarbonyl, n-butoxythiocarbonyl, tert-butoxythiocarbonyl, pentyloxythiocarbonyl, hexyloxythiocarbonyl, 2-ethylhexyloxythiocarbonyl, lauryloxythiocarbonyl, stearyloxythiocarbonyl group, cyclohexyloxythiocarbonyl and the like.

Examples of the substituted alkoxythiocarbonyl group (alkoxythiocarbonyl group having a substituent) include an alkoxythiocarbonyl group in which at least one hydrogen atom of the aforementioned alkoxythiocarbonyl group is substituted with the aforementioned substituent.

[0068]

Examples of the aryloxythiocarbonyl group optionally having a substituent as a substituent include an aryloxythiocarbonyl group and a substituted aryloxythiocarbonyl group. The aryloxythiocarbonyl group is, for example, an aryloxythiocarbonyl group having 7 to 20 carbon

atoms, and its specific examples include phenoxythiocarbonyl, naphthyloxythiocarbonyl and the like.

Examples of the substituted aryloxythiocarbonyl group (aryloxythiocarbonyl group having a substituent) include an aryloxythiocarbonyl group in which at least one hydrogen atom of the aryloxythiocarbonyl group is substituted with the aforementioned substituent.

[0069]

Examples of the aralkyloxythiocarbonyl group optionally having a substituent as a substituent include an aralkyloxythiocarbonyl group and a substituted aralkyloxythiocarbonyl group. The aralkyloxythiocarbonyl group is, for example, an aralkyloxythiocarbonyl group having 8 to 20 carbon atoms, and its specific examples include benzyloxythiocarbonyl, phenethyloxythiocarbonyl, 9-fluorenylmethyloxythiocarbonyl and the like.

Examples of the substituted aralkyloxythiocarbonyl group (aralkyloxythiocarbonyl group having a substituent) include an aralkyloxythiocarbonyl group in which at least one hydrogen atom of the aforementioned aralkyloxythiocarbonyl group is substituted with the aforementioned substituent.

[0070]

Examples of the alkylthiocarbonyl group optionally having a substituent as a substituent include an alkylthiocarbonyl group and a substituted alkylthiocarbonyl group. The alkylthiocarbonyl group is, for example, an alkylthiocarbonyl group of a carbon number of 2 to 20, which may be straight-chain, branched, or cyclic, and its specific examples include methylthiocarbonyl, ethylthiocarbonyl, n-propylthiocarbonyl,

2-propylthiocarbonyl, n-butylthiocarbonyl, tert-butylthiocarbonyl, pentylthiocarbonyl, hexylthiocarbonyl, 2-ethylhexylthiocarbonyl, laurylthiocarbonyl, stearylthiocarbonyl, cyclohexylthiocarbonyl and the like.

Examples of the substituted alkylthiocarbonyl group (alkylthiocarbonyl group having a substituent) include an alkylthiocarbonyl group in which at least one hydrogen atom of the alkylthiocarbonyl group is substituted with the aforementioned substituent.

[0071]

Examples of the arylthiocarbonyl group optionally having a substituent as a substituent include an arylthiocarbonyl group and a substituted arylthiocarbonyl group. The arylthiocarbonyl group is, for example, an arylthiocarbonyl group having 7 to 20 carbon atoms, and its specific examples include phenylthiocarbonyl, naphthylthiocarbonyl and the like.

Examples of the substituted arylthiocarbonyl group (arylthiocarbonyl group having a substituent) include an arylthiocarbonyl group in which at least one hydrogen atom of the arylthiocarbonyl group is substituted with the aforementioned substituent.

[0072]

Examples of the aralkylthiocarbonyl group optionally having a substituent as a substituent include an aralkylthiocarbonyl group and a substituted aralkylthiocarbonyl group. The aralkylthiocarbonyl group is, for example, an aralkylthiocarbonyl group having 8 to 20 carbon atoms, and its specific examples include benzylthiocarbonyl,

phenethylthiocarbonyl, 9-fluorenylmethylthiocarbonyl and the like.

Examples of the substituted aralkylthiocarbonyl group (aralkylthiocarbonyl group having a substituent) include an aralkylthiocarbonyl group in which at least one hydrogen atom of the aforementioned aralkylthiocarbonyl group is substituted with the aforementioned substituent.

[0073]

Examples of the carbamoyl group optionally having a substituent include a carbamoyl group and a substituted carbamoyl group. Examples of the substituted carbamoyl group include a carbamoyl group in which one or two hydrogen atoms of the amino group in a carbamoyl group are substituted with a substituent such as a hydrocarbon group optionally having a substituent and the like. The hydrocarbon group optionally having a substituent may be the same as the hydrocarbon group optionally having a substituent explained as a protecting group in R^1 in the general formula (2). Examples of the substituted carbamoyl group include N-methylcarbamoyl, N,N-diethylcarbamoyl, N-phenylcarbamoyl and the like.

[0074]

Examples of the substituted phosphino group include a phosphino group in which one or two hydrogen atoms of the phosphino group are substituted with a substituent such as a hydrocarbon group optionally having a substituent and the like. The hydrocarbon group optionally having a substituent may be the same as the hydrocarbon group optionally having a substituent explained as a protecting group in R^1 in the general formula (2). Examples of the substituted phosphino group

include dimethylphosphino, diethylphosphino, diphenylphosphino, methylphenylphosphino and the like.

[0075]

Inter alia, the protecting group represented by R^1 is preferably an acyl group optionally having a substituent, an alkoxycarbonyl group optionally having a substituent, an aryloxycarbonyl group optionally having a substituent, or an aralkyloxycarbonyl group optionally having a substituent.

[0076]

As a group having no α-proton represented by R^2, a group which does not isomerize an imine compound represented by the general formula (2) is preferable. Examples of the group having no α-proton include a tertiary alkyl group optionally having a substituent, an aryl group optionally having a substituent, a heterocyclic group optionally having a substituent and an acyl group optionally having a substituent.

Examples of the tertiary alkyl group optionally having a substituent include a tertiary alkyl group and a substituted tertiary alkyl group.

[0077]

The tertiary alkyl group is, for example, a tertiary alkyl group having 4 to 20 carbon atoms, and its specific examples include tert-butyl, tert-pentyl, tert-hexyl and the like.

Examples of the substituted tertiary alkyl group (tertiary alkyl group having a substituent) include a tertiary alkyl group in which at least one hydrogen atom of the tertiary alkyl group is substituted with a substituent. The substituent may be the same as the substituent explained in a protecting group in R^1. The substituted tertiary alkyl group is, for example, a

substituted tertiary alkyl group which is substituted with an aryl group, for example, an aralkyl group having 9 to 20 carbon atoms, and its specific examples include α,α-dimethylbenzyl and the like. Inter alia, the aralkyl group is preferably an aralkyl group having 9 to 15 carbon atoms.

The aryl group optionally having a substituent may be the same as the aryl group optionally having a substituent explained in the hydrocarbon group optionally having a substituent in a protecting group in R^1. In addition, the heterocyclic group optionally having a substituent and the acyl group optionally having a substituent may be the same as respective groups explained in a protecting group in R^1.

[0078]

The acyl group optionally having a substituent in a group having no α-proton is, for example, an acyl optionally having a substituent explained in a protecting group in R^1, and its specific examples include a group represented by R^bCO- (R^b represents a hydrocarbon group optionally having a substituent, a heterocyclic group optionally having a substituent, an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent, an aralkyloxy group optionally having a substituent, a heteroaryloxy group optionally having a substituent, an alkylthio group optionally having a substituent, an arylthio group optionally having a substituent, an aralkylthio group optionally having a substituent, a heteroarylthio group optionally having a substituent or a substituted amino group). The hydrocarbon group optionally having a substitutent and the heterocyclic group optionally having a substituent represented by R^b may be the same as the

hydrocarbon group optionally having a substituent and the heterocyclic group optionally having a substituent explained in a protecting group in R^1. In addition, the alkoxy group optionally having a substituent, the aryloxy group optionally having a substituent, the aralkyloxy group optionally having a substituent, the heteroaryloxy group optionally having a substituent, the alkylthio group optionally having a substituent, the arylthio group optionally having a substituent, the aralkylthio group optionally having a substituent, the heteroarylthio group optionally having a substituent and the substituted amino group may be the same as respective groups explained in a substituent in the hydrocarbon group optionally having a substituent in a protecting group in R^1.

[0079]

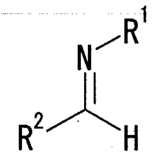
Examples of the unsaturated hydrocarbon group include an alkenyl group optionally having a substituent, an alkynyl group optionally having a substituent and an alkadienyl group optionally having a substituent. The alkenyl group optionally having a substituent, the alkynyl group optionally having a substituent and the alkadienyl group optionally having a substituent may be the same as respective groups explained in the hydrocarbon group optionally having a substituent in a protecting group in R^1.

[0080]

Examples of the imine compound represented by the general formula (2) used in the present invention include the following compound.

Exemplified compound 2-1:

[0081]



R^1 :Ac, Bz, Boc, Z, Fmoc, Troc, etc.

R^2 :Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py, t-Bu, $-CH=CH-CH_2$, 1-Propynyl, Ac, -COOMe, -COOEt, -COOBn, etc.

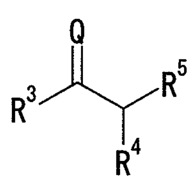
[0082]

In the above embodiment, Ac represents an acetyl group, Bz represents a benzoyl group, Boc represents a tert-butoxycarbonyl group, Z represents a benzyloxycarbonyl group, Fmoc represents a fluorenylmethoxycarbonyl group, Troc represents a 2,2,2-trichloroethoxycarbonyl group, Ph represents a phenyl group, Nap represents a naphthyl group, Py represents a pyridyl group, t-Bu represents a tert-butyl group, Me represents a methyl group, Et represents an ethyl group, and Bn represents a benzyl group, respectively (hereinafter the same).

[0083]

Examples of the nucleophilic compound (provided that trialkylsilyl vinyl ethers are excluded) used in the present invention include a compound represented by the general formula (3):

[0084]



(3)

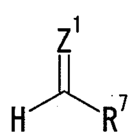
[0085]

(wherein R^3 represents a hydrogen atom, a hydrocarbon group

optionally having a substituent, a heterocyclic group optionally having a substituent, an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent, an aralkyloxy group optionally having a substituent or a substituted amino group; R^4 and R^5 each independently represent a hydrogen atom, a hydrocarbon group optionally having a substituent, a heterocyclic group optionally having a substituent, EWG^1 (EWG^1 represents an electron withdrawing group), an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent, an aralkyloxy group optionally having a substituent, an alkylthio group optionally having a substituent, an arylthio group optionally having a substituent, an aralkylthio group optionally having a substituent, or a hydroxy group; Q represents a group giving a tautomer of the compound represented by the general formula (3); and R^3 and R^4, R^3 and R^5, or R^4 and R^5 may be taken together to form a ring),

a compound represented by the general formula (5):

[0086]



(5)

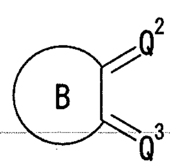
[0087]

(wherein R^7 represents a hydrogen atom, a hydrocarbon group optionally having a substituent, a heterocyclic group optionally having a substituent, an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent or an aralkyloxy group optionally having a substituent, an alkylthio group optionally having a substituent, an arylthio group optionally having a substituent, an

aralkylthio group optionally having a substituent or EWG^2 (EWG^2 represents an electron withdrawing group), and Z^1 represents N_2, $P(R^8)_3$ (three R^8s are the same or different, and represent a hydrogen atom, a hydrocarbon group optionally having a substituent, a heterocyclic group optionally having a substituent, an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent or an aralkyloxy group optionally having a substituent) or CR^9R^{10} (R^9 and R^{10} each independently represent a hydrogen atom, a hydrocarbon group optionally having a substituent, a heterocyclic group optionally having a substituent, an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent, an aralkyloxy group optionally having a substituent, an alkylthio group optionally having a substituent, an arylthio group optionally having a substituent, an aralkylthio group optionally having a substituent, an amino group or a substituted amino group, provided that either one of R^9 and R^{10} represents an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent, an aralkyloxy group optionally having a substituent, an alkylthio group optionally having a substituent, an arylthio group optionally having a substituent, an aralkylthio group optionally having a substituent, an amino group or a substituted amino group)),for example,

a compound represented by the general formula (7):

[0088]



(7)

[0089]

(wherein ring B represents an aliphatic ring or an aliphatic heterocycle; Q^2 and Q^3 each independently represent an oxygen atom, NR^{17} (R^{17} represents a hydrogen atom or a protecting group) or a sulfur atom).

[0090]

The hydrocarbon group optionally having a substituent and the heterocyclic group optionally having a substituent represented by R^3, R^4 and R^5 in the general formula (3) may be the same as respective groups explained as a protecting group in R^1 in the general formula (2).

[0091]

The alkoxy group optionally having a substituent, the aryloxy group optionally having a substituent, the aralkyloxy group optionally having a substituent, and the substituted amino group represented by R^3, and the alkoxy group optionally having a substituent, the aryloxy group optionally having a substituent, the aralkyloxy group optionally having a substituent, the alkylthio group optionally having a substituent, the arylthio group optionally having a substituent and the aralkylthio group optionally having a substituent represented by R^4 and R^5 may be the same as respective groups explained in a substituent in the hydrocarbon group optionally having a substituent and the like explained as a protecting group in R^1 in the general formula (2).

[0092]

EWG^1 represented by R^4 and R^5 represents an electron withdrawing group. Examples of the electron withdrawing group include an acyl group optionally having a substituent, an

alkoxycarbonyl group optionally having a substituent, an aryloxycarbonyl group optionally having a substituent, an aralkyloxycarbonyl group optionally having a substituent, an alkoxythiocarbonyl group optionally having a substituent, an aryloxythiocarbonyl group optionally having a substituent, an aralkyloxythiocarbonyl group optionally having a substituent, an alkylthiocarbonyl group optionally having a substituent, an arylthiocarbonyl group optionally having a substituent, an aralkylthiocarbonyl group optionally having a substituent, a carbamoyl group optionally having a substituent, a cyano group, a nitro group, a halogen atom and the like.

The acyl group optionally having a substituent, the alkoxycarbonyl group optionally having a substituent, the aryloxycarbonyl group optionally having a substituent, the aralkyloxycarbonyl group optionally having a substituent, the alkylthiocarbonyl group optionally having a substituent, the arylthiocarbonyl group optionally having a substituent, the aralkylthiocarbonyl group optionally having a substituent, the alkoxythiocarbonyl group optionally having a substituent, the aryloxythiocarbonyl group optionally having a substituent, the aralkyloxythiocarbonyl group optionally having a substituent, the alkylthiocarbonyl group optionally having a substituent, the arylthiocarbonyl group optionally having a substituent, the aralkylthiocarbonyl group optionally having a substituent, the carbamoyl group optionally having a substituent and the halogen atom in the electron withdrawing group may be the same as respective groups explained in a substituent in the hydrocarbon group optionally having a substituent and the like explained as a protecting group in R^1 in the general formula (2).

[0093]

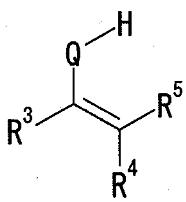
When the electron withdrawing group is an alkoxycarbonyl group optionally having a substituent, an aryloxycarbonyl group optionally having a substituent, an aralkyloxycarbonyl group optionally having a substituent, an alkoxythiocarbonyl group optionally having a substituent, an aryloxythiocarbonyl group optionally having a substituent, an aralkyloxythicarbonyl group optionally having a substituent, an alkylthiocarbonyl group optionally having a substituent, an arylthiocarbonyl group optionally having a substituent, an aralkylthiocarbonyl group optionally having a substituent, a carbamoyl group optionally having a substituent or the like, the electron withdrawing group is represented by the formula, for example, R^h-C(=Z^1)- (R^h represents an alkoxy group optionally having a substituent, an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent, an aralkyloxy group optionally having a substituent, an alkylthio group optionally having a substituent, an arylthio group optionally having a substituent, an aralkylthio group optionally having a substituent, an amino group, a substituted amino group or the like, and Z^1 represents an oxygen atom or a sulfur atom (the alkoxy group optionally having a substituent, the aryloxy group optionally having a substituent, the aralkyloxy group optionally having a substituent, the alkylthio group optionally having a substituent, the arylthio group optionally having a substituent, the aralkylthio group optionally having a substituent and the substituted amino group may be the same as respective groups explained in the substituents in the hydrocarbon group optionally having a substituent and the like

explained as a protecting group in R^1 in the general formula (2))).

[0094]

The group represented by Q giving a tautomer of the compound represented by the general formula (3) is not particularly limited as far as it is a group capable of giving a compound such that a compound represented by the general formula (3) is a tautomer represented, for example, by the general formula (3-1):

[0095]



(3-1)

[0096]

(wherein R^3 to R^5 and Q are the same as defined above).

Examples of the group represented by Q capable of giving a tautomer of a compound represented by the general formula (3) include an oxygen atom, NR^6 (R^6 represents a hydrogen atom or a protecting group) and a sulfur atom.

[0097]

The protecting group represented by R^6 in NR^6 may be the same as the protecting group explained of R^1 in the general formula (2).

[0098]

When R^3 and R^4, R^3 and R^5, or R^4 and R^5 are taken together to form a ring in the general formula (3), examples of the formed ring include a 4- to 8-membered aliphatic ring which may be monocyclic, polycyclic, or fused cyclic. In addition, -O-,

-NH-, a carbonyl group (C=O), a thiocarbonyl group (C=S) or the like may be contained in the carbon chain constituting a ring. Examples of the ring in the case of ring formation include a cyclopentane ring, a cyclohexane ring, for example, a 5- to 7-membered lactone ring, for example, a 5- to 7-membered lactam ring and the like.

[0099]

In the general formula (3), it is preferable that either one of R^4 and R^5 is EWG^1 (EWG^1 is the same as defined above). In addition, in the case where R^3 and R^4, R^3 and R^5, or R^4 and R^5 are taken together to form a ring, R^5 may be EWG^1 when R^3 and R^4 are taken together to form a ring, and R^4 may be EWG^1 when R^3 and R^5 are taken together to form a ring. Furthermore, when R^4 and R^5 are taken together to form a ring, the formed ring may have EWG^1, or a group derived from EWG^1 may be present. Examples of the group derived from EWG^1 include a carbonyl group, a thiocarbonyl group and the like.

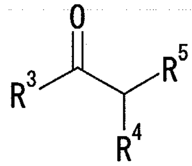
[0100]

Examples of the compound represented by the general formula (3) used in the present invention include the following compounds.

Exemplified compound 3-1:

1) Exemplified compound 3-1-1:

[0101]



R3: H, Me, Et, iPr, Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py, OMe, OEt, SMe, SEt, NMe_2, NEt_2, etc.

R4: H, Me, Et, iPr, Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py, etc.

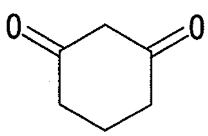
R5: EWG1

EWG1 : -CHO, Ac, Bz,
-COOMe, -COOEt, $-COOBu^t$, -COOBn, -COSMe,
$-CONH_2$, $-CONMe_2$, $-CONEt_2$,
-CN, $-NO_2$, $-PO(OMe)_2$, $-SO_2Me$, etc.

[0102]

1) Exemplified compound 3-1-2:

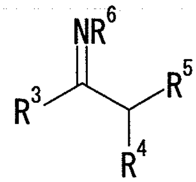
[0103]



[0104]

Exemplified compound 3-2:

[0105]



R^3: H, Me, Et, iPr, Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py, OMe, OEt, SMe, SEt, NMe_2, NEt_2, etc.

R^4: H, Me, Et, iPr, Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py, etc.

R^5: EWG^1

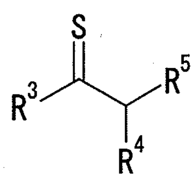
EWG^1 : -CHO, Ac, Bz,
-COOMe, -COOEt, $-COOBu^t$, -COOBn, -COSMe,
$-CONH_2$, $-CONMe_2$, $-CONEt_2$,
-CN, $-NO_2$, $-PO(OMe)_2$, $-SO_2Me$, etc.

R^6: H, Me, Et, iPr, Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py, COMe, COPh, COOMe, COOPh, $COOCH_2Ph$, $COOBu^t$, $CONMe_2$, etc.

[0106]

Exemplified compound 3-3:

[0107]



R^3: H, Me, Et, iPr, Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py, OMe, OEt, SMe, SEt, NMe_2, NEt_2, etc.

R^4: H, Me, Et, iPr, Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py, etc.

R^5: EWG^1

EWG^1 : -CHO, Ac, Bz,
-COOMe, -COOEt, $-COOBu^t$, -COOBn, -COSMe,
$-CONH_2$, $-CONMe_2$, $-CONEt_2$,
-CN, $-NO_2$, $-PO(OMe)_2$, $-SO_2Me$, etc.

[0108]

In the above embodiment, ^iPr represents a 2-propyl group, and Bu^t represents a tert-butyl group (hereinafter the same).

[0109]

In the general formula (5), the hydrocarbon group

optionally having a substituent, the heterocyclic group optionally having a substituent, the alkoxy group optionally having a substituent, the aryloxy group optionally having a substituent, the aralkyloxy group optionally having a substituent, the alkylthio group optionally having a substituent, the arylthio group optionally having a substituent and the aralkylthio group optionally having a substituent represented by R^7 may be the same as respective groups explained in R^4 and R^5 in the general formula (3). In addition, an electron withdrawing group represented by EWG^2 may be the same as an electron withdrawing group represented by EWG^1 explained in R^4 and R^5 in the general formula (3).

[0110]

In $P(R^8)_3$ in Z^1, three R^8s are the same or different, and represent a hydrogen atom, a hydrocarbon group optionally having a substituent, a heterocyclic group optionally having a substituent, an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent or an aralkyloxy group optionally having a substituent. The hydrocarbon group optionally having a substituent and the heterocyclic group optionally having a substituent may be the same as respective groups explained as a protecting group in R^1 in the general formula (2). In addition, the alkoxy group optionally having a substituent, the aryloxy group optionally having a substituent, and the aralkyloxy group optionally having a substituent may be the same as respective groups explained as a substituent in a protecting group in R^1.

In CR^9R^{10}, the hydrocarbon group optionally having a substituent and the heterocyclic group optionally having a

substituent represented by R^9 and R^{10} may be the same as respective groups explained as a protecting group in R^1 in the general formula (2). In addition, the alkoxy group optionally having a substituent, the aryloxy group optionally having a substituent, the aralkyloxy group optionally having a substituent, the alkylthio group optionally having a substituent, the arylthio group optionally having a substituent, the aralkylthio group optionally having a substituent and the substituted amino group may be the same as respective groups explained as a substituent in the hydrocarbon group optionally having a substituent of the protecting group in R^1 in the general formula (2). In addition, in CR^9R^{10}, either one of R^9 and R^{10} represents an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent, an aralkyloxy group optionally having a substituent, an alkylthio group optionally having a substituent, an arylthio group optionally having a substituent, an aralkylthio group optionally having a substituent, an amino group or a substituted amino group.

R^7 in the general formula (5) is preferably an electron withdrawing group represented by EWG^2.

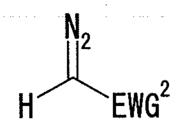
[0111]

Examples of the compound represented by the general formula (5) include the following compounds.

Exemplified compound 6-1:

1) Exemplified compound 6-1-1:

[0112]

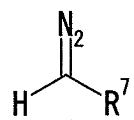


EWG^2 :-CHO, Ac, Bz,
-COOMe, -COOEt, -COOBu^t, -COOBn, -COSMe,
-CONH$_2$, -CONMe$_2$, -CONEt$_2$,
-CN, -NO$_2$, -PO(OMe)$_2$, -SO$_2$Me, etc.

[0113]

2) Exemplified compound 6-1-2:

[0114]

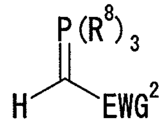


R^7 :-OMe, -OEt, -OBn, -SMe, -SEt, -SBn, etc.

[0115]

Exemplified compound 6-2:

[0116]



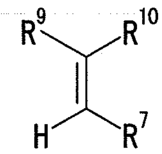
R^8 :Me, Et, iPr, Ph, 4-Me-Ph, -OMe, -OEt, -OBn, etc.

EWG^2 :-CHO, Ac, Bz,
-COOMe, -COOEt, -COOBu^t, -COOBn, -COSMe,
-CONH$_2$, -CONMe$_2$, -CONEt$_2$,
-CN, -NO$_2$, -PO(OMe)$_2$, -SO$_2$Me, etc.

[0117]

Exemplified compound 6-3:

[0118]



R^9, R^{10} :H, Me, Et, iPr, Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py, OMe, OEt, SMe, SEt, NMe2, NEt2, etc.

R^7 :-CHO, Ac, Bz,
-OMe, -OEt, -OBn, -SMe, -SEt, -SBn,
-COOMe, -COOEt, $-COOBu^t$, -COOBn, -COSMe,
$-CONH_2$, $-CONMe_2$, $-CONEt_2$,
-CN, $-NO_2$, $-PO(OMe)_2$, $-SO_2Me$, etc.

[0119]

In the exemplified compound 6-3, it is preferable that either one of R^9 and R^{10} is at least one member selected from the group consisting of an alkoxy group optionally having a substituent such as OMe, OEt, SMe, Set, NMe, NEt and the like, an aryloxy group optionally having a substituent, an aralkyloxy group optionally having a substituent, an alkylthio group optionally having a substituent, an arylthio group optionally having a substituent, an aralkylthio group optionally having a substituent, an amino group and a substituted amino group.

[0120]

In the general formula (7), examples of the aliphatic ring represented by ring B include an aliphatic ring having 4 to 20 carbon atoms. Examples of the alicyclic ring include a monocyclic aliphatic ring, and a polycyclic or fused aliphatic ring. Examples of the aliphatic ring include a cyclobutane ring, a cyclopentane ring, a cyclohexane ring, a tetrahydronaphthalene ring, a perhydronaphthalene ring and the like. Inter alia, the aliphatic ring is preferably an aliphatic heterocyclic ring having 5 to 14 carbon atoms.

Examples of the aliphatic heterocycle include a 5- to

8-membered, preferably 5- or 6-membered monocyclic aliphatic heterocycle, and a polycyclic or fused aliphatic heterocycle having 2 to 20 carbon atoms, which contains at least one, preferably 1 to 3 heteroatom(s) such as a nitrogen atom, an oxygen atom and/or a sulfur atom as a heteroatom. Examples of the aliphatic heterocycle include a piperazine ring, a morpholine ring, a lactone ring, a lactam ring and the like. Inter alia, the aliphatic heterocycle is preferably an aliphatic heterocycle having 2 to 14 carbon atoms.

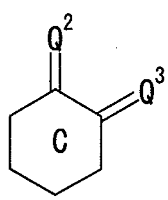
[0121]

NR^{17} represented by Q^2 and Q^3 may be the same as NR^6 represented by Q in the general formula (3).

[0122]

Examples of the compound represented by the general formula (7) include a compound represented by the general formula (7-1):

[0123]



(7-1)

[0124]

wherein the ring C represents a cyclohexane ring, and Q^2 and Q^3 are the same as defined above.)

[0125]

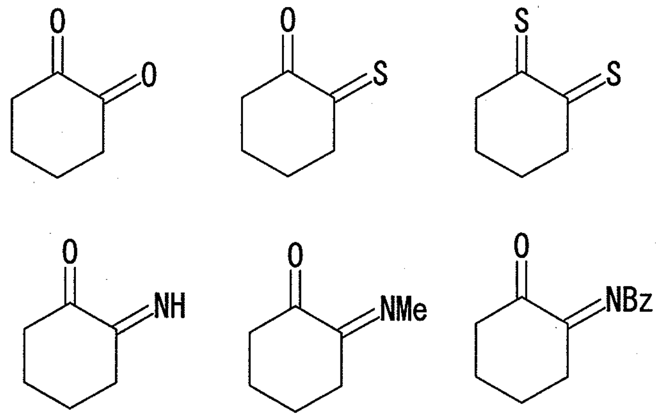
In the general formula (7-1), a cyclohexane ring represented by the ring C may be monocyclic, polycyclic, or fused cyclic and, further, the cyclohexane ring may have a substituent explained in the hydrocarbon group optionally having a substituent in the general formula (2).

[0126]

Examples of the compound represented by the general formula (7-1) include the following compounds.

Exemplified compound 7-1:

[0127]



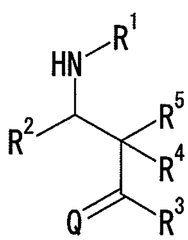
[0128]

As imines and nucleophilic compounds used in the present invention, commercially available products may be used, or those that have been appropriately prepared may be used.

[0129]

Examples of the amines obtained by the process of the present invention include an amine represented by the general formula (4):

[0130]



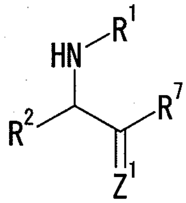
(4)

[0131]

(wherein R^1 to R^5 and Q are the same as defined above),

an amine represented by the general formula (6):

[0132]



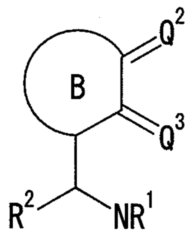
(6)

[0133]

(wherein R^1, R^2, R^7 and Z^1 are the same as defined above),

an amine represented by the general formula (8):

[0134]



(8)

[0135]

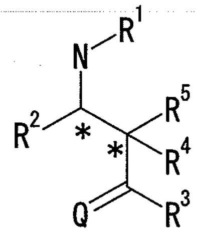
(wherein R^1, R^2, Q^2 and Q^3 are the same as defined above), and the like.

The amines obtained by these processes of the present invention are a chiral compound.

[0136]

When an optically active phosphoric acid derivative is used as a phosphoric acid derivative represented by the general formula (1), the amine obtained by the process of the present invention is preferably an optically active amine. As the optically active amine, inter alia, the amine represented by the general formula (4) is preferably an optically active amine represented by the general formula (4a):

[0137]



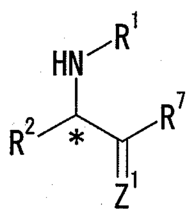
(4a)

[0138]

(wherein * represents an asymmetric carbon atom, and R^1 to R^5 and Q are the same as defined above)

and, inter alia, the amine represented by the general formula (6) is preferably an optically active amine represented by the general formula (6a):

[0139]



(6a)

[0140]

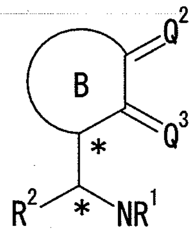
(wherein * represents an asymmetric carbon atom, and R^1, R^2, R^7 and Z^1 are the same as defined above).

In the general formula (4a), when R^4 and R^5 are each the same group, the carbon atom to which R^4 and R^5 are attached is not an asymmetric carbon atom.

[0141]

When an optically active phosphoric acid derivative is used as a phosphoric acid derivative represented by the general formula (1), an optically active amine represented by the general formula (8a):

[0142]



(8a)

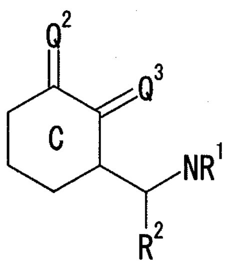
[0143]

(wherein a ring B, Q^2, Q^3 and * are the same as defined above) is obtained as the amine represented by the general formula (8).

[0144]

Examples of the amines represented by the general formula (8) include an amine represented by the general formula (8-1):

[0145]



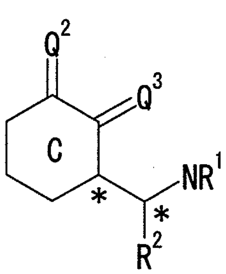
(8-1)

[0146]

(wherein a ring C, Q^2 and Q^3 are the same as defined above).

When an optically active phosphoric acid derivative is used as a phosphoric acid derivative represented by the general formula (1), for example, an optically active amine represented by the general formula (8a-1):

[0147]



(8a-1)

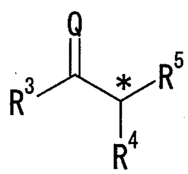
[0148]

(wherein ring C, Q^2, Q^3 and * are the same as defined above) is obtained as the amine represented by the general formula (8-1). The optically active amines represented by the general formula (8a-1) are a preferable one of the optically active amines represented by the general formula (8a).

[0149]

Among the compounds represented by the general formula (3), an optically active compound (i.e. compound in which R^4 and R^5 are not the same) represented by the general formula (3a):

[0150]



(3a)

[0151]

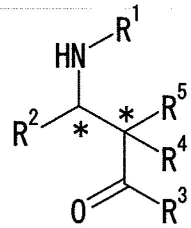
(wherein R^3 to R^5, Q and * are the same as defined above) may be used as the nucleophilic compound in the process of the present invention.

[0152]

Examples of the amines represented by the general formula (4a) obtained by the process of the present invention include compounds represented by the following formulae.

Exemplified compound 4a-1:

[0153]



R^1 :Ac, Bz, Boc, Z, Fmoc, Troc, etc.

R^2 :Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py,
t-Bu, $-CH=CH-CH_2$, 1-Propynyl,
Ac, -COOMe, -COOEt, -COOBn, etc.

R^3:, R^4: H, Me, Et, iPr, Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py,
OMe, OEt, OBn, SMe, SEt, SBn, etc.

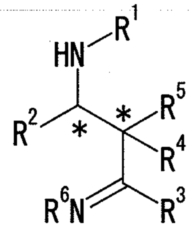
R^5:EWG^1

EWG^1 :-CHO, Ac, Bz,
-COOMe, -COOEt, $-COOBu^t$, -COOBn, -COSMe,
$-CONH_2$, $-CONMe_2$, $-CONEt_2$,
-CN, $-NO_2$, $-PO(OMe)_2$, $-SO_2Me$, etc.

[0154]

Exemplified compound 4a-2:

[0155]



R^1 :Ac, Bz, Boc, Z, Fmoc, Troc, etc.

R^2 :Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py,
t-Bu, $-CH=CH-CH_2$, 1-Propynyl,
Ac, -COOMe, -COOEt, -COOBn, etc.

R^3:, R^4: H, Me, Et, iPr, Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py,
OMe, OEt, OBn, SMe, SEt, SBn, etc.

R^5:EWG^1

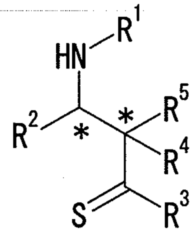
EWG^1 :-CHO, Ac, Bz,
-COOMe, -COOEt, $-COOBu^t$, -COOBn, -COSMe,
$-CONH_2$, $-CONMe_2$, $-CONEt_2$,
-CN, $-NO_2$, $-PO(OMe)_2$, $-SO_2Me$, etc.

R^6:H, Me, Et, iPr, Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py,
OMe, OEt, OBn, SMe, SEt, SBn, etc.

[0156]

Exemplified compound 4a-3:

[0157]



R^1 :Ac, Bz, Boc, Z, Fmoc, Troc, etc.

R^2 :Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py, t-Bu, $-CH=CH-CH_2$, 1-Propynyl, Ac, -COOMe, -COOEt, -COOBn, etc.

R^3:, R^4: H, Me, Et, iPr, Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py, OMe, OEt, OBn, SMe, SEt, SBn, etc.

R^5: EWG^1

EWG^1 :-CHO, Ac, Bz, -COOMe, -COOEt, $-COOBu^t$, -COOBn, -COSMe, $-CONH_2$, $-CONMe_2$, $-CONEt_2$, -CN, $-NO_2$, $-PO(OMe)_2$, $-SO_2Me$, etc.

[0158]

In the amines represented by the general formula (4a) obtained according to the process of the present invention, the carbon atom to which R^4 and R^5 are attached is not an asymmetric carbon atom when R^4 and R^5 are the same group.

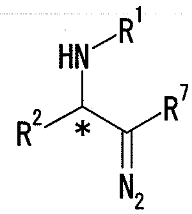
[0159]

Examples of the amines represented by the general formula (6a) obtained according to the process of the present invention include compounds represented by the following formulae.

Exemplified compound 6a-1:

1) Exemplified compound 6a-1-1

[0160]



R^1 :Ac, Bz, Boc, Z, Fmoc, Troc, etc.

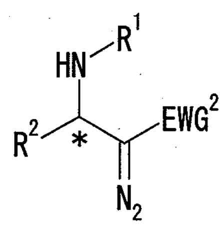
R^2 :Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py,
t-Bu, -CH=CH-CH_2, 1-Propynyl,
Ac, -COOMe, -COOEt, -COOBn, etc.

R^7 :-OMe, -OEt, -OBn, -SMe, -SEt, -SBn, etc.

[0161]

2) Exemplified compound 6a-1-2

[0162]



R^1 :Ac, Bz, Boc, Z, Fmoc, Troc, etc.

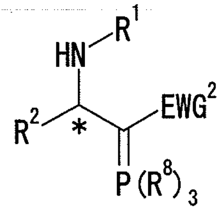
R^2 :Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py,
t-Bu, -CH=CH-CH_2, 1-Propynyl,
Ac, -COOMe, -COOEt, -COOBn, etc.

EWG^2 :-CHO, Ac, Bz,
-OMe, -OEt, -OBn, -SMe, -SEt, -SBn,
-COOMe, -COOEt, -$COOBu^t$, -COOBn, -COSMe,
-$CONH_2$, -$CONMe_2$, -$CONEt_2$,
-CN, -NO_2, -$PO(OMe)_2$, -SO_2Me, etc.

[0163]

Exemplified compound 6a-2:

[0164]



R^1 :Ac, Bz, Boc, Z, Fmoc, Troc, etc.

R^2 :Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py,
t-Bu, $-CH=CH-CH_2$, 1-Propynyl,
Ac, -COOMe, -COOEt, -COOBn, etc.

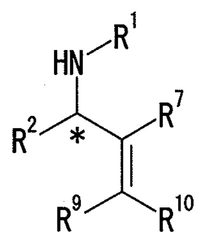
R^8 :Me, Et, iPr, Ph, 4-Me-Ph, OMe, OEt,
OBn, SMe, SEt, SBn, etc.

EWG^2 :-CHO, Ac, Bz,
-COOMe, -COOEt, $-COOBu^t$, -COOBn, -COSMe,
$-CONH_2$, $-CONMe_2$, $-CONEt_2$,
-CN, $-NO_2$, $-PO(OMe)_2$, $-SO_2Me$, etc.

[0165]

Exemplified compound 6a-3:

[0166]



R^1 :Ac, Bz, Boc, Z, Fmoc, Troc, etc.

R^2 :Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py,
t-Bu, $-CH=CH-CH_2$, 1-Propynyl,
Ac, -COOMe, -COOEt, -COOBn, etc.

R^9, R^{10} :H, Me, Et, iPr, Ph, 4-Me-Ph, 4-Cl-Ph, Nap, Py,
OMe, OEt, SMe, SEt, NMe2, NEt2, etc.

R^{11} :Me, Et, iPr, Ph, 4-Me-Ph, etc.

R^7 :-CHO, Ac, Bz,
-OMe, -OEt, -OBn, -SMe, -SEt, -SBn,
-COOMe, -COOEt, $-COOBu^t$, -COOBn, -COSMe,
$-CONH_2$, $-CONMe_2$, $-CONEt_2$,
-CN, $-NO_2$, $-PO(OMe)_2$, $-SO_2Me$, etc.

[0167]

In the phosphoric acid derivative represented by the general formula (1) used in the present invention, examples of the spacer represented by A^1 include an alkylene group optionally having a substituent, an arylene group optionally having a substituent, a divalent organic group optionally having a substituent and the like.

[0168]

Examples of the alkylene group optionally having a substituent include an alkylene group and a substituted alkylene group. The alkylene group is, for example, an alkylene group having 1 to 10 carbon atoms, which may be straight-chain, branched, or cyclic, and examples of the alkylene group include methylene, ethylene, trimethylene, propylene, tetramethylene, butylene, 1,2-dimethylethylene, pentylene, hexylene, 1,2-cyclohexylene and the like.

[0169]

Examples of the substituted alkylene group include an alkylene group in which at least one hydrogen atom of the aforementioned alkylene group is substituted with a substituent. The substituent may be the same as the substituent explained in the hydrocarbon group optionally having a substituent explained as a protecting group in R^1 in the general formula (2). Examples of the substituted alkylene group include 1,2-diphenylethylene, 1,2-di(4-methylphenyl)ethylene, 1,2-dicyclohexylethylene, 1,3-dioxolane-4,5-diyl and the like.

[0170]

Examples of the arylene group optionally having a

substituent include an arylene group and a substituted arylene group. The arylene group is, for examples, an arylene group having 6 to 20 carbon atoms, and examples of the arylene group include phenylene, biphenyldiyl, binaphthalenediyl and the like. Examples of the substituted arylene group include an arylene group in which at least one hydrogen atom of the arylene group is substituted with a substituent. The substituent may be the same as the substituent explained in the hydrocarbon group optionally having a substituent explained as a protecting group in R^1 in the general formula (2).

[0171]

These divalent organic groups may have at least one group such as an oxygen atom, a carbonyl group and the like at the terminal of the organic group or an arbitrary position in the chain.

[0172]

When the phosphoric acid derivative represented by the general formula (1) is an optically active phosphoric acid derivative, the spacer represented by A^1 is preferably a spacer having an optically active site. Examples of the spacer having an optically active site include 1,2-dimethylethylene, 1,2-cyclohexylene, 1,2-diphenylethylene, 1,2-di(4-methylphenyl)ethylene group, 1,2-dicyclohexylethylene, 1,3-dioxolane-4,5-diyl, diphenyldiyl, binaphthalenediyl and the like.

[0173]

Examples of the divalent nonmetal atom represented by X^1 and X^2 include an oxygen atom, a sulfur atom and the like. Examples of the divalent nonmetal atomic group include $-NR^{13}-$

(R^{13} represents a hydrogen atom, a hydrocarbon group optionally having a substituent or an acyl group optionally having a substituent), and $-CR^{15}R^{16}-$ {R^{15} and R^{16} each independently represent a hydrogen atom, a hydrocarbon group optionally having a substituent or EWG^3 (EWG^3 represents an electron withdrawing group), provided that either one of R^{15} and R^{16} is EWG^3}.

[0174]

In the divalent nonmetal atomic group, the hydrocarbon group optionally having a substituent and the acyl group optionally having a substituent in $-NE^{13}-$ may be the same as respective groups explained as a protecting group in R^1 in the general formula (2).

[0175]

The hydrocarbon group optionally having a substituent represented by R^{15} or R^{16} may be the same as the hydrocarbon group optionally having a substituent explained as a protecting group in R^1 in the general formula (2).

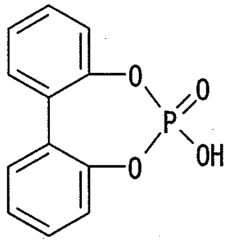
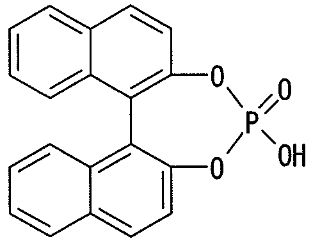
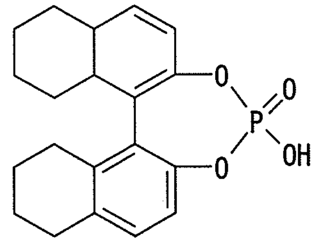
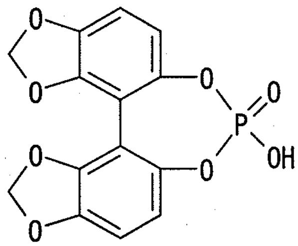
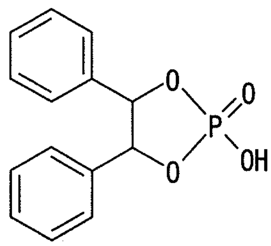
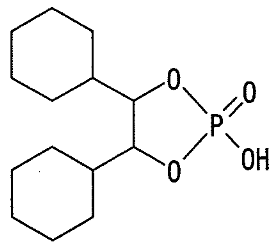
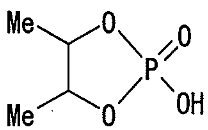
EWG^3 may be the same as EWG^1 explained in R^4 and R^5 in the general formula (3).

[0176]

Examples of the phosphoric acid derivative represented by the general formula (1) include compounds represented by the following formulae.

Exemplified compound 1-1:

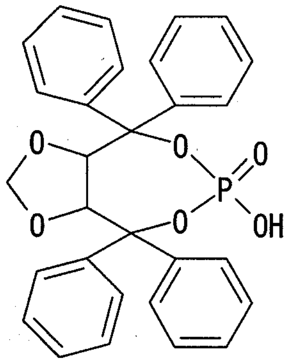
[0177]

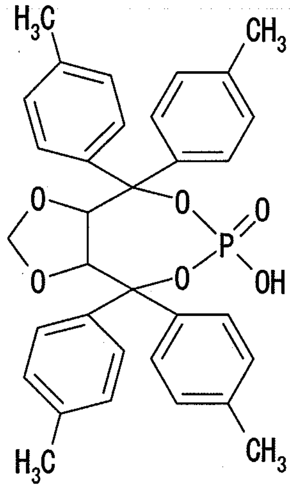








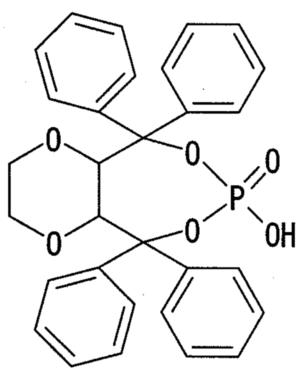
[0178]

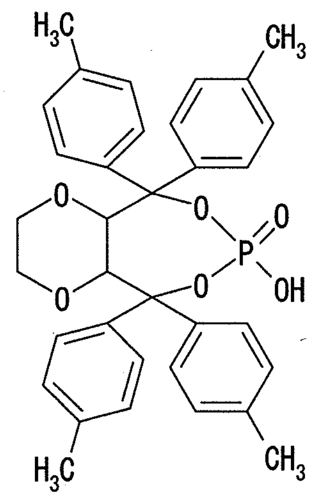
Exemplified compound 1-2:

[0179]





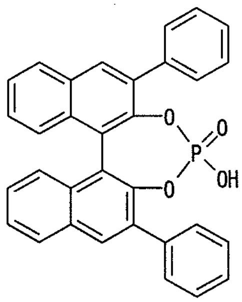


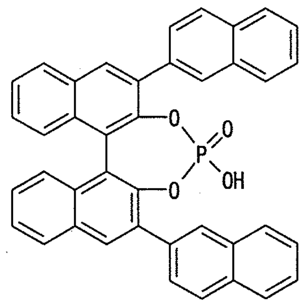


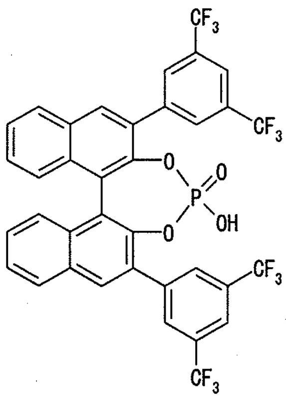
[0180]

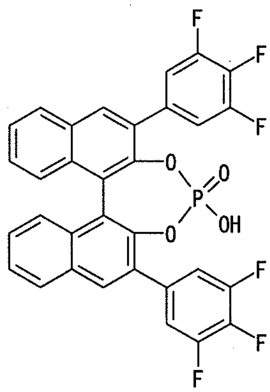
Exemplified compound 1-3:

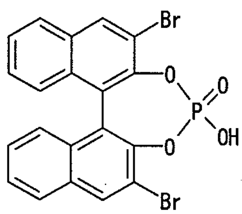
[0181]

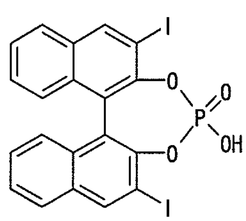


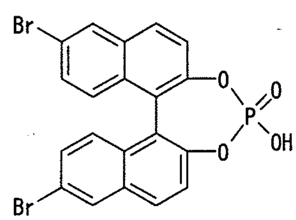




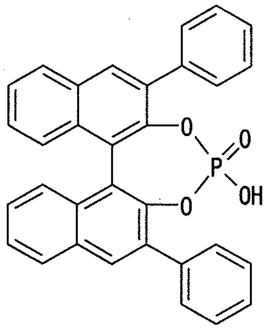


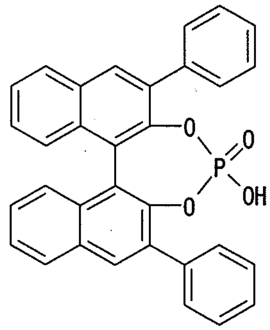


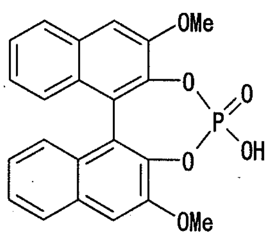


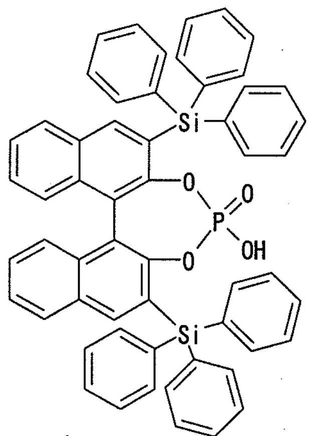


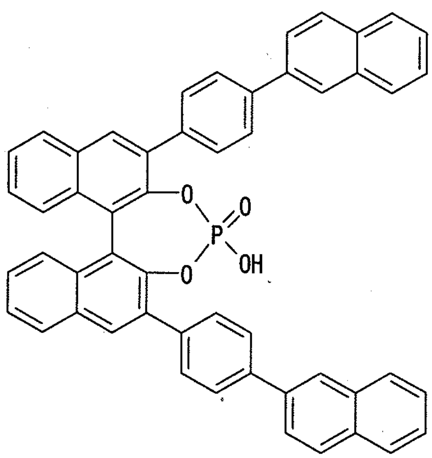
[0182]



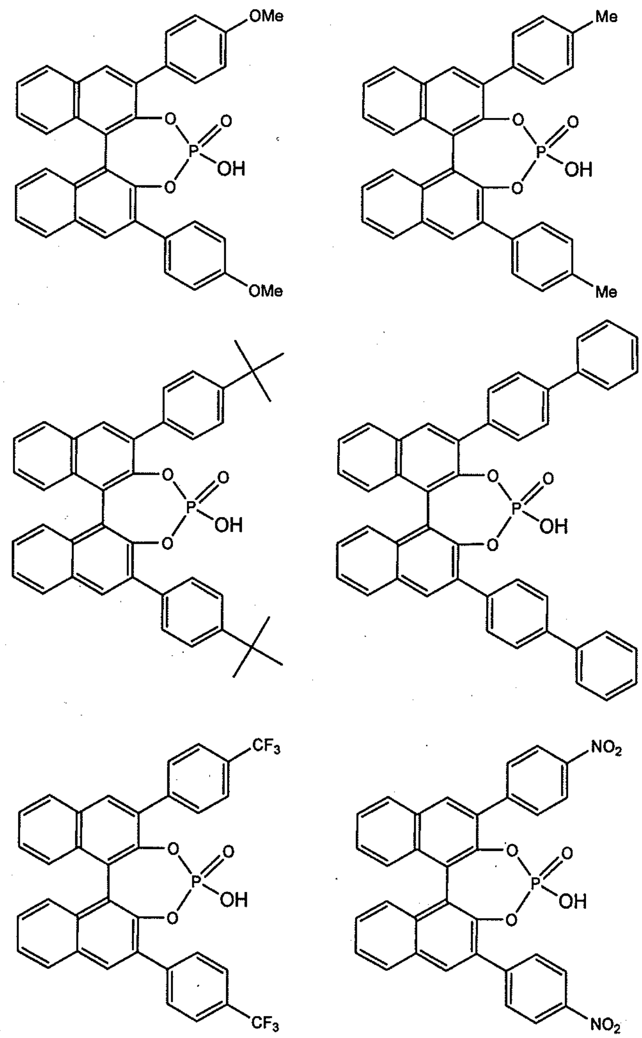








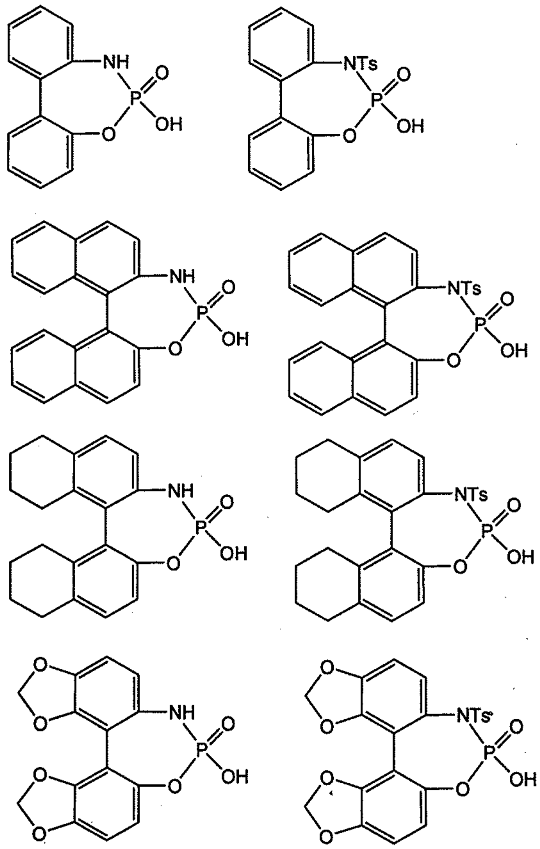
[0183]



[0184]

Exemplified compound 1-4:

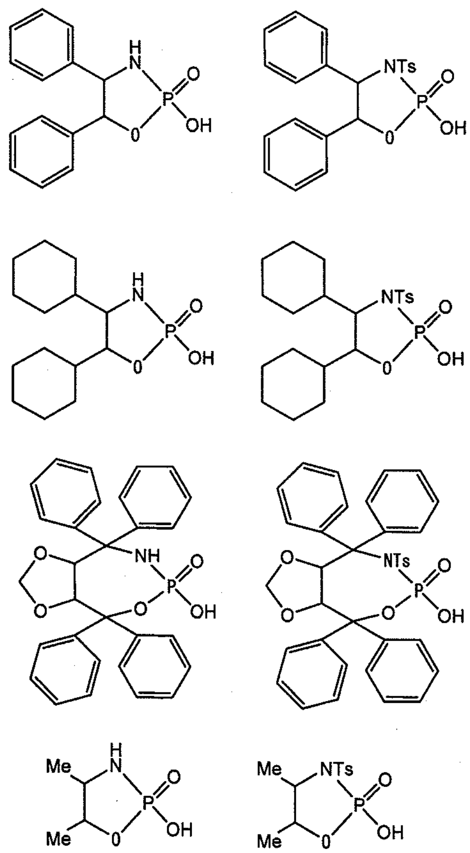
[0185]



[0186]

Exemplified compound 1-5:

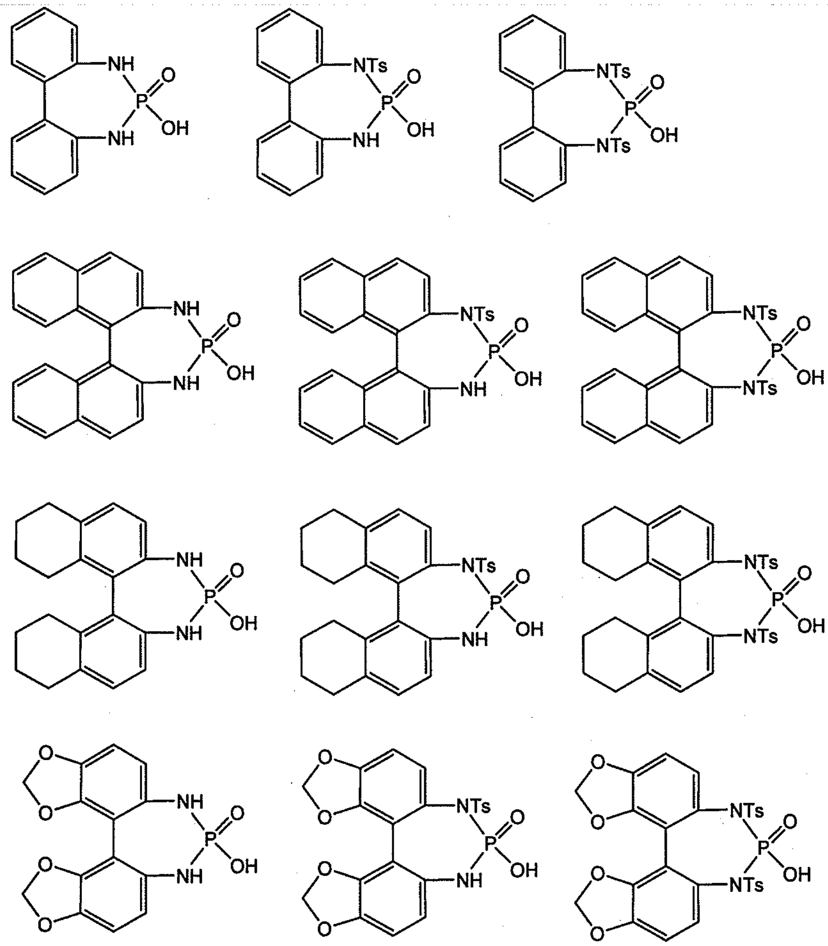
[0187]



[0188]

Exemplified compound 1-6:

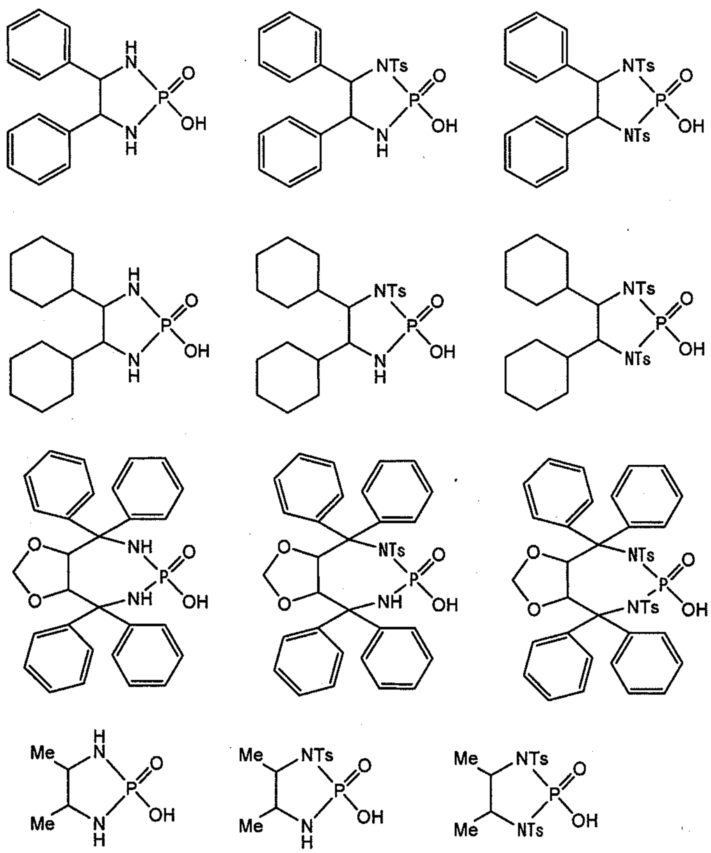
[0189]



[0190]

Exemplified compound 1-7:

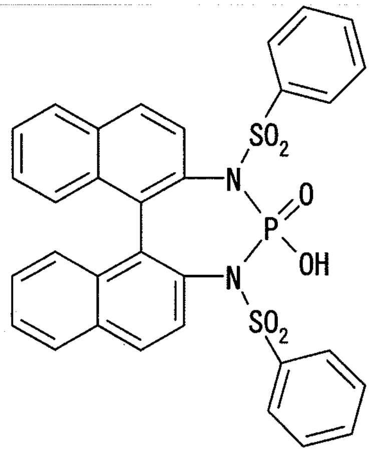
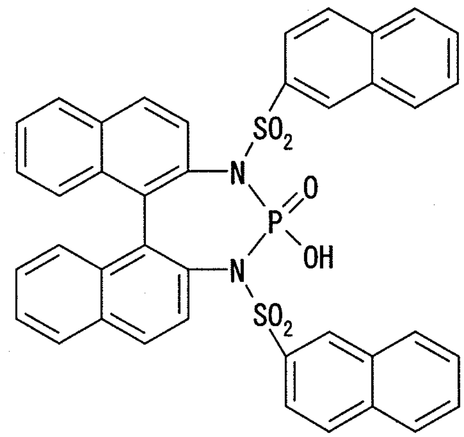
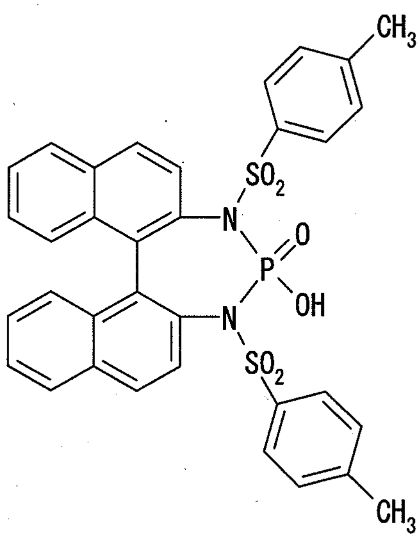
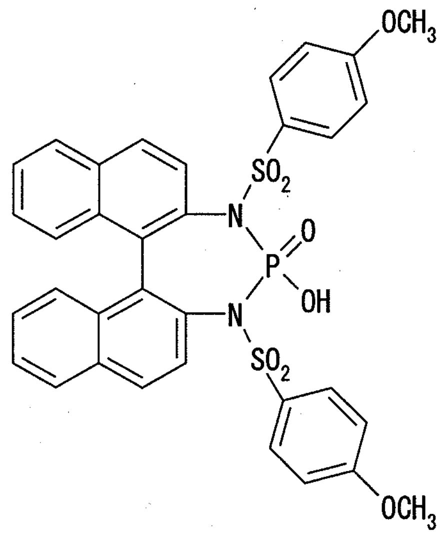
[0191]



[0192]

Exemplified compound 1-8:

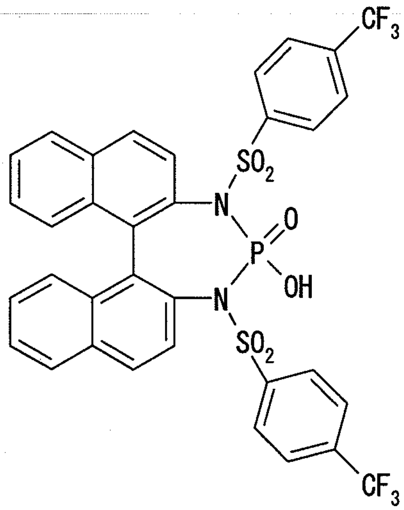
[0193]

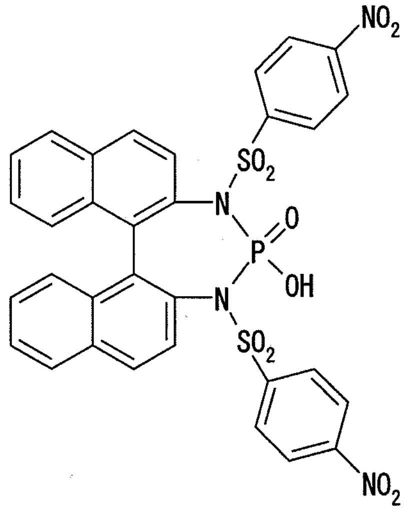





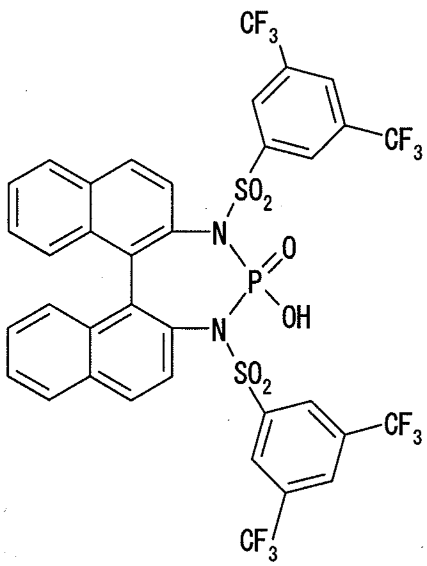
[0194]

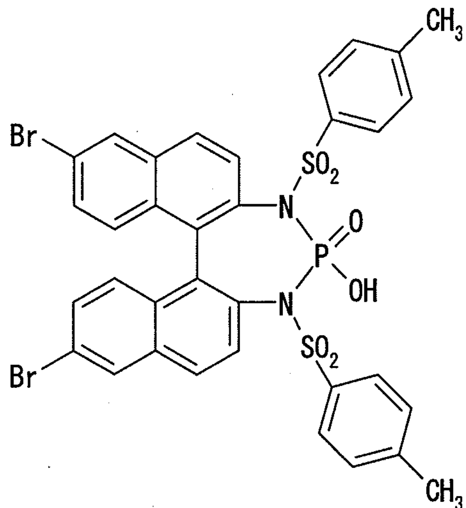
Exemplified compound 1-9:

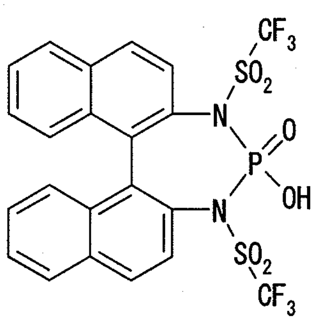
[0195]







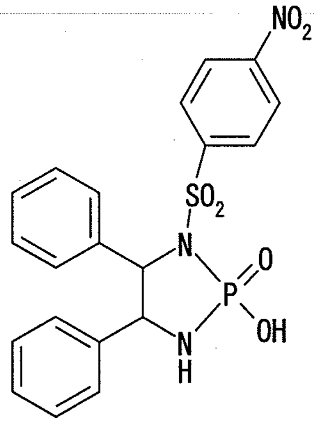


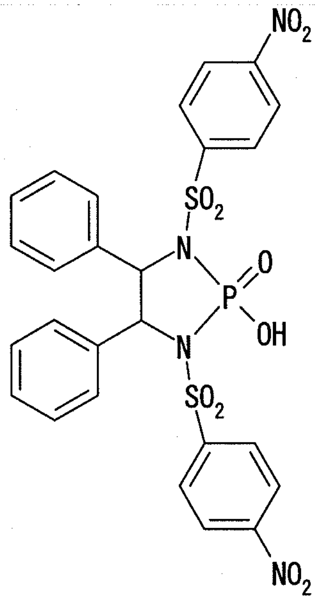


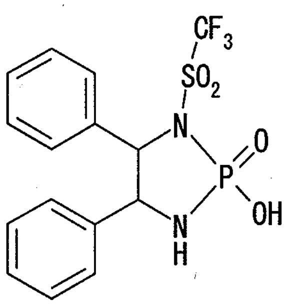
[0196]

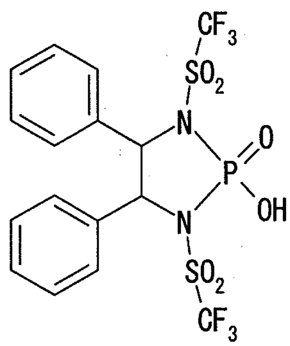
Exemplified compound 1-10:

[0197]





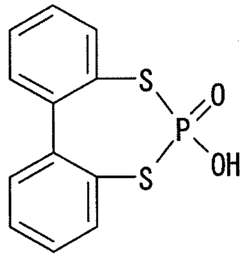
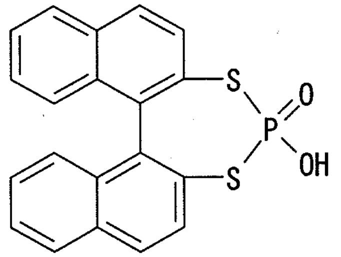
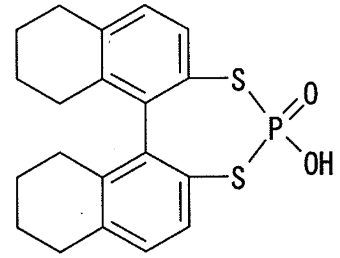
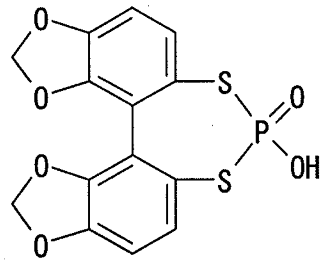
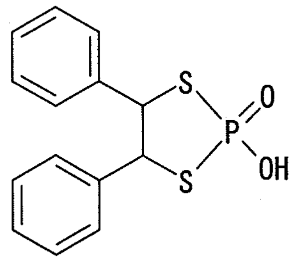
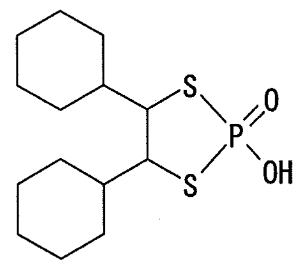
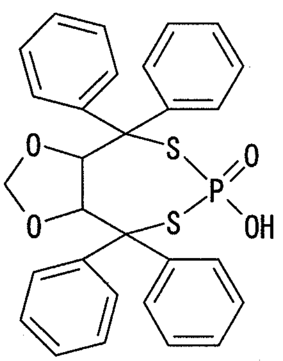
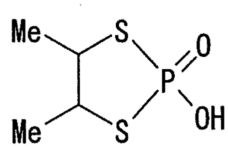




[0198]

Exemplified compound 1-11:

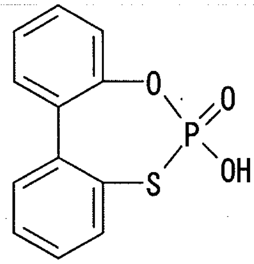
[0199]

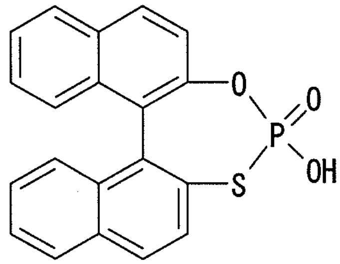









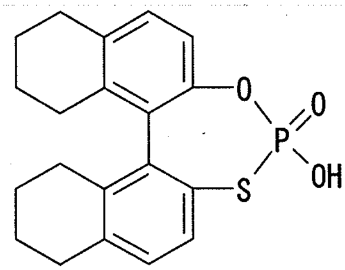
[0200]

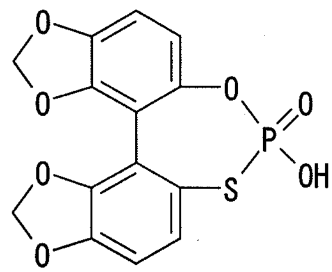
Exemplified compound 1-12:

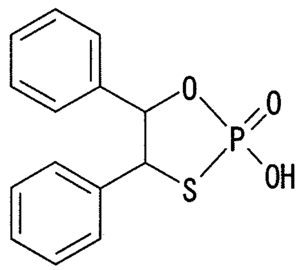
[0201]

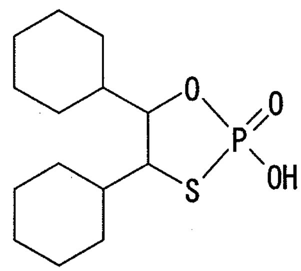


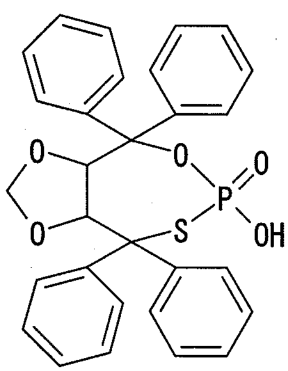


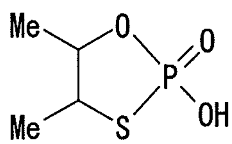








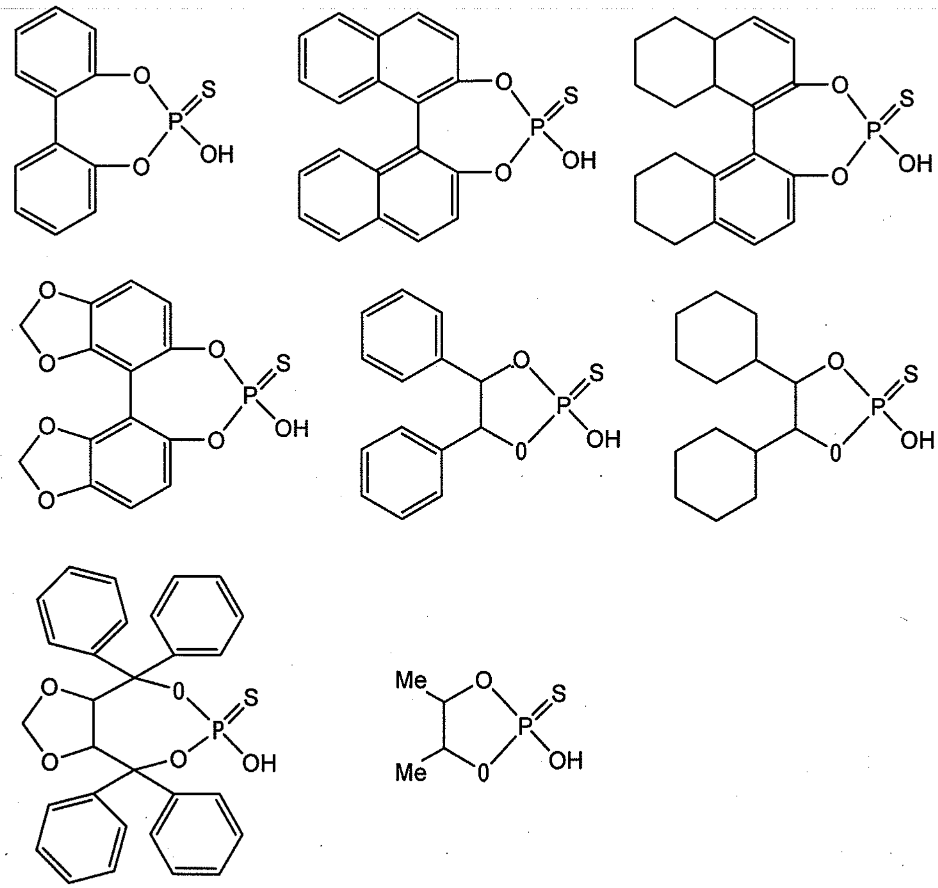




[0202]

Exemplified compound 1-13:

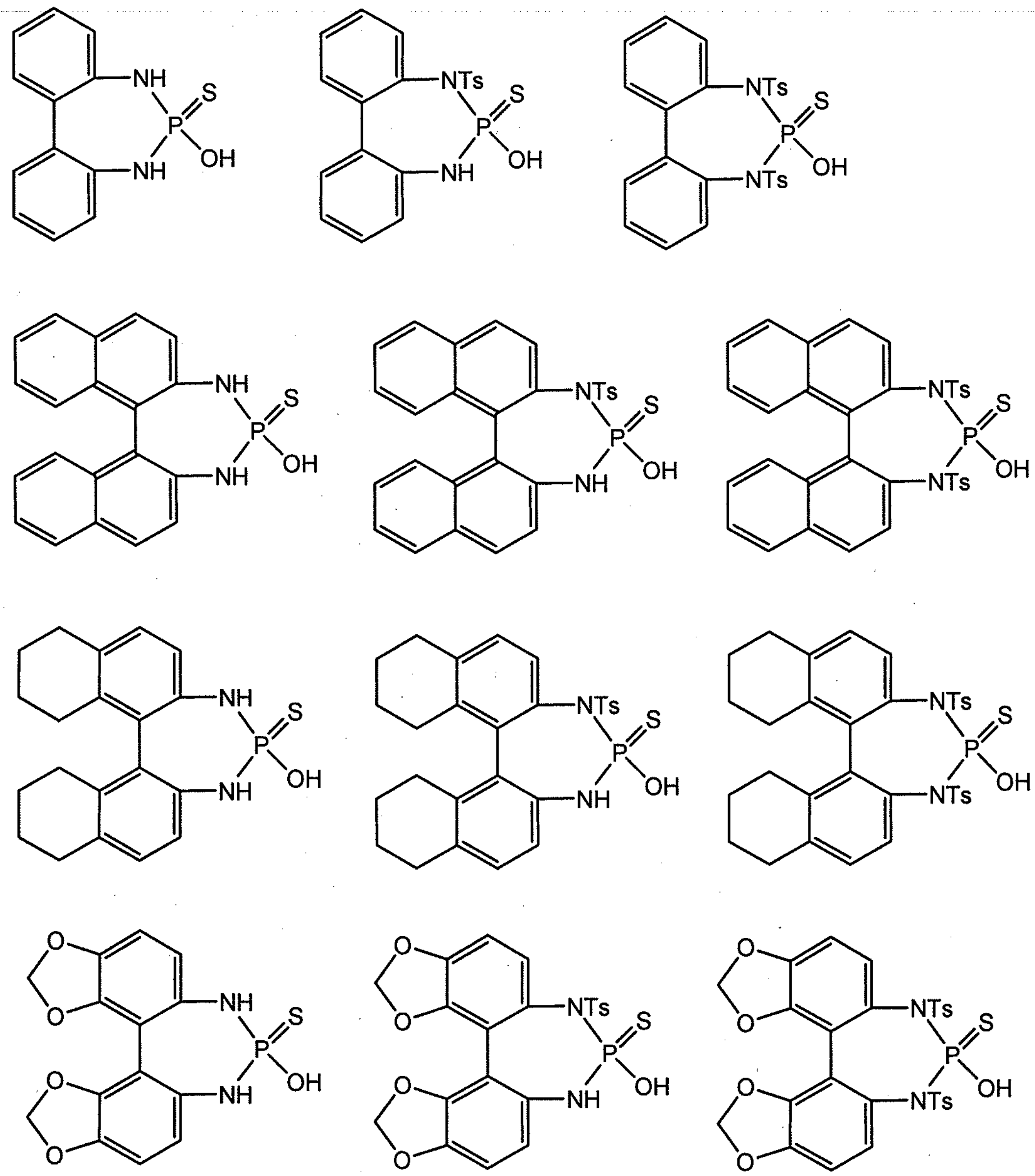
[0203]



[0204]

Exemplified compound 1-14:

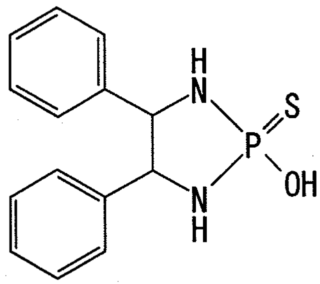
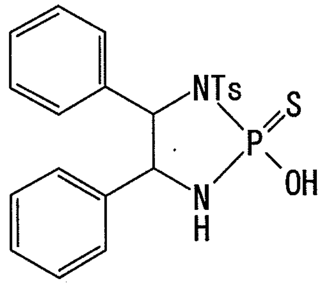
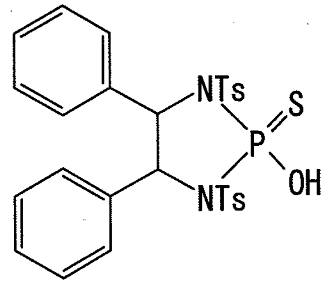
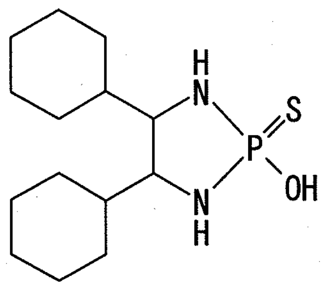
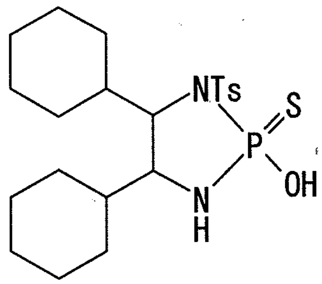
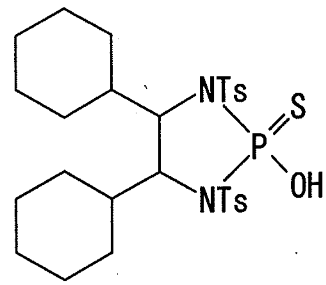
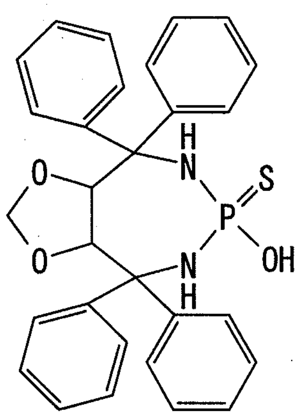
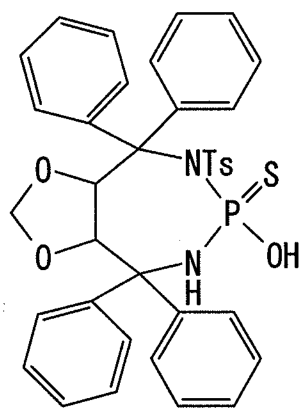
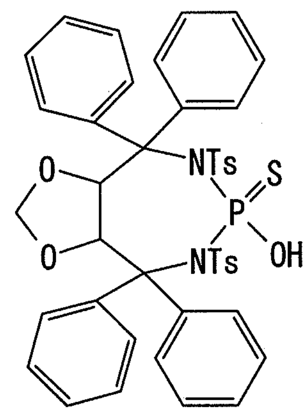
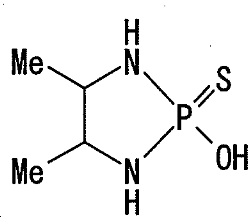
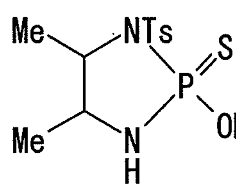
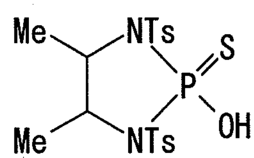
[0205]



[0206]

Exemplified compound 1-15:

[0207]

[0208]

These phosphoric acid derivatives represented by the general formula (1) and the like of the present invention include phosphoric acid derivatives in which -OH of the phosphoric acid moiety is a metal salt or an ammonium salt.

Examples of the metal salt include salts of an alkali metal

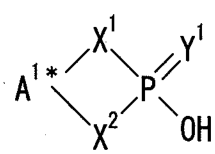
such as lithium, sodium, potassium, rubidium, cesium and the like, an alkali earth metal such as magnesium, calcium, strontium, barium and the like, and the like.

Examples of the ammonium salt include salts of ammonia, aliphatic amines such as methylamine, ethylamine, propylamine, butylamine, cyclohexylamine, dimethylamine, diethylamine, diisopropylamine, triethylamine, tripropylamine, diisopropylethylamine, di(2-ethylhexyl)amine, hexadecylamine, tri-n-butylamine, N-methylmorpholine and the like, aromatic amines such as N,N-dimethylaniline, pyridine, 4-dimethylaminopyridine and the like, saturated heterocyclic amines such as piperidine and the like, and the like.

[0209]

In the process of the present invention, when an optically active compound is prepared, the phosphoric acid derivative represented by the general formula (1) is preferably an optically active phosphoric acid derivative represented by the general formula (1-1):

[0210]



(1-1)

[0211]

(wherein A^{1*} represents a spacer having an optically active site, and X^1, X^2 and Y^1 are the same as defined above).

[0212]

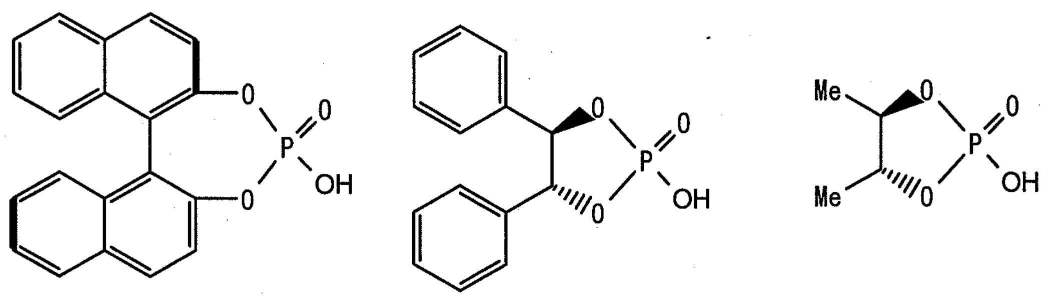
In the general formula (1-1), examples of the spacer having an optically active site represented by A^{1*} include a spacer having an optically active site among the spacers represented by A^1 in the general formula (1).

[0213]

Examples of the optically active phosphoric acid derivative represented by the general formula (1-1) include a compound which is optically active among phosphoric acid derivatives exemplified as an example of the phosphoric acid derivative represented by the general formula (1). Representative examples of the optically active phosphoric acid derivative represented by the general formula (1-1) include compounds represented by the following formulas:

Exemplified compound 1-1-1:

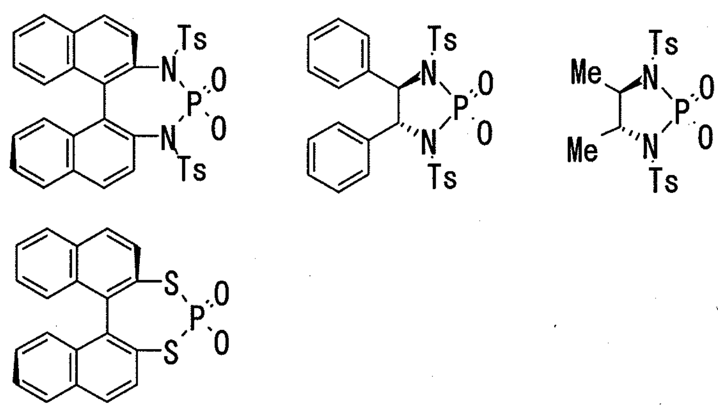
[0214]



[0215]

Exemplified compound 1-1-2:

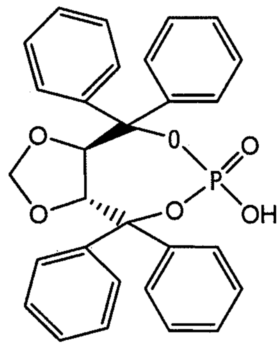
[0216]



[0217]

Exemplified compound 1-1-3:

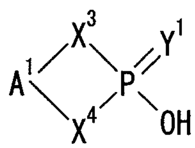
[0218]



[0219]

As the phosphoric acid derivative represented by the general formula (1), a phosphoric acid derivative represented by the general formula (1a):

[0220]



(1a)

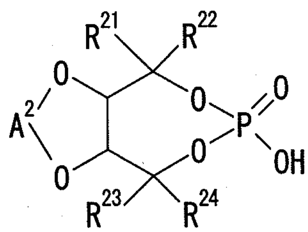
[0221]

(wherein A^1 represents a spacer; X^3 and X^4 each independently represent an oxygen atom, $-NR^{13}-$ (R^{13} represents a hydrogen atom, a hydrocarbon group optionally having a substituent or an acyl group optionally having a substituent), a sulfur atom or $-CR^{15}R^{16}-$ {R^{15} and R^{16} each independently represent a hydrogen atom, a hydrocarbon group optionally having a substituent or EWG^3 (EWG^3 represents an electron withdrawing group), provided that either one of R^{15} and R^{16} is EWG^3}, and Y^1 represents an oxygen atom or a sulfur atom, provided that when i) $X^3=X^4$, then X^3 and X^4 are $-NR^{13}-$ (R^{13} represents a hydrogen atom, a hydrocarbon group optionally having a substituent or an acyl group optionally having a substituent), a sulfur atom or $-CR^{15}R^{16}-$ and, when X^3 and X^4 are $-NR^{13}-$, then the $-NR^{13}-$ is $-NR^a-$ (R^a represents an acyl group derived from sulfonic acid), and that when ii) X^3 and X^4

are different, either one of X^3 and X^4 is $-NR^{13}-$, and the $-NR^{13}-$ is $-NR^a-$ (R^a represents an acyl group derived from sulfonic acid), and the other is an oxygen atom, $-NR^{13}-$ (R^{13} represents a hydrogen atom, a hydrocarbon group optionally having a substituent or an acyl group optionally having a substituent), a sulfur atom or $-CR^{15}R^{16}-$),

a phosphoric acid derivative represented by the general formula (1b):

[0222]



(1b)

[0223]

(wherein A^2 represents a spacer; and R^{21} to R^{24} each independently represent a hydrocarbon group optionally having a substituent or a heterocyclic group having a substituent),

and the like are preferable.

[0224]

In the general formula (1a), X^3 and X^4 each represent, independently, an oxygen atom, $-NR^{13}-$ (R^{13} represents a hydrogen atom, a hydrocarbon group optionally having a substituent or an acyl group optionally having a substituent), a sulfur atom or $-CR^{15}R^{16}-$ {R^{15} and R^{16} each independently represent a hydrogen atom, a hydrocarbon group optionally having a substituent or EWG^3 (EWG^3 represents an electron withdrawing group), provided that either one of R^{15} and R^{16} is EWG^3}, and Y^1 represents an oxygen atom or a sulfur atom, provided that when i) X^3=X^4, then X^3 and X^4 are $-NR^{13}-$ (R^{13} represents a hydrogen atom, a hydrocarbon group

optionally having a substituent or an acyl group optionally having a substituent), a sulfur atom or $-CR^{15}R^{16}-$ and, when X^3 and X^4 are $-NR^{13}-$, then the $-NR^{13}-$ is $-NR^a-$ (R^a represents an acyl group derived from sulfonic acid) and, when ii) X^3 and X^4 are different, then either one of X^3 and X^4 is $-NR^{13}-$, and the $-NR^{13}-$ is $-NR^a-$ (R^a represents an acyl group derived from sulfonic acid), and the other is an oxygen atom, $-NR^{13}-$ (R^{13} represents a hydrogen atom, a hydrocarbon group optionally having a substituent or an acyl group optionally having a substituent), a sulfur atom or $-CR^{15}R^{16}-$.

The acyl group derived from sulfonic acid represented by R^a may be the same as the acyl group derived from sulfoni c acid explained in the acyl group optionally having a substituent explained in a protecting group in R^1 in the general formula (2).

[0225]

Examples of the phosphoric acid derivative represented by the general formula (1a) include compounds exemplified in the Exemplified compounds 1-4 to 1-15.

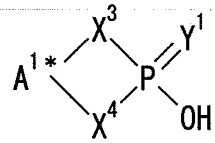
[0226]

Examples of the phosphoric acid derivative represented by the general formula (1b) include the compounds exemplified in the Exemplified compound 1-2.

[0227]

As the phosphoric acid derivatives represented by the general formula (1a) and the general formula (1b), an optically active phosphoric acid derivative represented by the general formula (1a-1):

[0228]



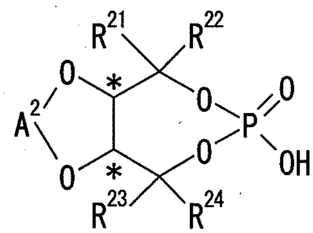
(1a-1)

[0229]

(wherein A^{1*}, X^3, X^4 and Y^1 are the same as defined above, provided that when X^3 is $-NR^{13}-$, then R^{13} in the NR^{13} and A^{1*} are not taken together to form a ring), and

an optically active phosphoric acid derivative represented by the general formula (1b-1):

[0230]



(1b-1)

[0231]

(wherein A^{2*} represents a spacer having an optically active site, and R^{21} to R^{24} are the same as defined above) are preferable.

[0232]

Examples of the phosphoric acid derivative represented by the general formula (1a-1) include compounds which are an optically active form among the phosphoric acid derivatives exemplified in the Exemplified compounds 1-4 to 1-15. Representative examples of the optically active phosphoric acid derivative represented by the general formula (1a-1) include a compound represented by the Exemplified compound 1-1-2.

[0233]

Examples of the phosphoric acid derivative represented by the general formula (1b-1) include compounds which are an optically active form among the phosphoric acid derivatives

exemplified in the Exemplified compound 1-2. Representative examples of the optically active phosphoric acid derivative represented by the general formula (1b-1) include the compound represented by Exemplified compound 1-1-3.

[0234]

The phosphoric acid derivative represented by the general formula (1) can be produced, for example, as follows.

[0235]

For example, the phosphoric acid derivative represented by the general formula (1) can be obtained by reacting a compound represented by the general formula (10):

[0236]

$H\text{-}X^1\text{-}A^1\text{-}X^2\text{-}H$ (10)

(wherein A^1, X^1 and X^2 are the same as defined above) with a phosphorylating agent.

[0237]

Examples of the compound represented by the general formula (10) include diols, aminoalcohols, diamines, dithiols, mercaptoalcohols, mercaptoamines and the like.

[0238]

Examples of the diols include a diol represented by the general formula (10-1):

[0239]

$HO\text{-}A^1\text{-}OH$ (10-1)

(wherein A^1 is the same as defined above).

[0240]

Examples of the diols include ethylene glycol, propylene glycol, catechol, 1,2-cyclohexanediol, 1,2-diphenylethylene glycol, 2,2′-dihydroxybiphenyl, 1,1′-bi-2-naphthol,

5,5′,6,6′,7,7′,8,8′-octahydro(1,1-binaphthalene)-2,2′-diol and the like.

[0241]

Examples of the aminoalcohols include an aminoalcohol represented by the general formula (10-2):

[0242]

$HO\text{-}A^{1}\text{-}NHR^{z1}$ (10-2)

(wherein R^{z1} represents a hydrogen atom, a hydrocarbon group optionally having a substituent or an acyl group optionally having a substituent, and A^{1} is as defined above).

The hydrocarbon group optionally having a substituent and the acyl group optionally having a substituent represented by the aforementioned R^{z1}, and R^{z2} to R^{z4} may be the same as respective groups explained in R^{13} in the $-NH^{13}$.

[0243]

Examples of the aminoalcohols include 2-aminoethanol, 1-amino-2-propanol, o-aminophenol, 1-amino-1,2-diphenylethyl alcohol, 2-amino-2′-hydroxybiphenyl, 2-amino-2′-hydroxybinaphthyl, 2-(N-(4-toluenesulfonyl)amino)-2′-hydroxybiphenyl, 2-(N-(4-toluenesulfonyl)amino)-2′-hydroxybinaphthyl and the like.

[0244]

Examples of the diamines include a diamine represented by the general formula (10-3):

[0245]

$R^{z2}HN\text{-}A^{1}\text{-}NHR^{z3}$ (10-3)

(wherein R^{z2} and R^{z3} each independently represent a hydrogen atom, a hydrocarbon group optionally having a substituent or an acyl group optionally having a substituent, and A^{1} is the same as

defined above).

[0246]

Examples of the diamines include an N-unsubstituted diamine such as ethylenediamine, 1,2-diaminocyclohexane, 1,2-dicyclohexylethylenediamine, 1,2-phenylenediamine, 2,2′-diaminobinaphthyl, 1,2-diphenylethylenediamine, 1,2-dinaphthylethylenediamine and the like; N-mono-substituted diamines such as N-benzenesulfonyl-1,2-phenylenediamine, N-methanesulfonyl-1,2-phenylenediamine, N-(4-toluenesulfonyl)-1,2-phenylenediamine, N-benzenesulfonyl-1,2-diphenylethylenediamine, N-methanesulfonyl-1,2-diphenylethylenediamine, N-(4-toluenesulfonyl)-1,2-diphenylethylenediamine and the like; N-di-substituted-diamines such as N,N′-dibenzenesulfonyl-1,2-phenylenediamine, N,N′-dimethanesulfonyl-1,2-phenylenediamine, N,N′-di(4-toluenesulfonyl)-1,2-phenylenediamine, N,N′-dibenzenesulfonyl-1,2-diphenylethylenediamine, N,N′-dimethanesulfonyl-1,2-diphenylethylenediamine, N,N′-di(4-toluenesulfonyl)-1,2-diphenylethylenediamine, N,N′-dibenzenasulfonyl-1,2-dicyclohexylethylenediamine, N,N′-dimethanesulfonyl-1,2-dicyclohexylethylenediamine, N,N′-di(4-toluenesulfonyl)-1,2-dicyclohexylethylenediamine, 2,2-di(N,N′-dibenzenesulfonyl)aminobinaphthyl, 2,2-di(N,N′-dimethanesulfonyl)aminobinaphthyl, 2,2-di(N,N′-di(4-toluenesulfonyl))aminobinaphthyl and the like, and the like.

[0247]

Examples of the dithiols include a dithiol represented by the general formula (10-4):

[0248]

HS-A^1-SH (10-4)

(wherein A^1 is the same as defined above).

[0249]

Examples of the dithiols include ethanedithiol, 1,2-propanedithiol and the like.

[0250]

Examples of the mercaptoalcohols include a mercaptoalcohol represented by the general formula (10-5):

[0251]

HS-A^1-OH (10-5)

(wherein A^1 is the same as defined above).

[0252]

Examples of the mercaptoalcohols include 2-mercaptoethanols, 2-hydroxythiophenol and the like.

[0253]

Examples of the mercaptoamines include a mercaptoamine represented by the general formula (10-6):

[0254]

HS-A^1-NHR^{z4} (10-6)

(wherein R^{z4} represents a hydrogen atom, a hydrocarbon group optionally having a substituent or an acyl group optionally having a substituent, and A^1 is as defined above).

[0255]

Examples of the mercaptoamines include 2-aminothiophenol, 2-(N-(4-toluenesulfonyl)amino)thiophenol and the like.

[0256]

It is preferable that, as compounds represented by the general formula (10), an optically active compound represented

by the general formula (10a):

[0257]

$H\text{-}X^1\text{-}A^{1*}\text{-}X^2\text{-}H$ (10a)

(wherein A^{1*}, X^1 and X^2 are the same as defined above) is used in order to obtain the optically active phosphoric acid derivative represented by the general formula (1-1). This is also true in the compound represented by the general formulae (10-1) to (10-6).

[0258]

As the optically active compound represented by the general formula (10a), any optically active compounds can be used as far as it is in an optically active form among compounds such as diols, aminoalcohols, diamines, dithiols, mercaptoalcohols, mercaptoamines and the like exemplified as the compound represented by the general formula (10). As the optically active compound represented by the general formula (10a), representative examples of the diols, aminoalcohols and diamines include an optically active diol such as (1R, 2R)-1,2-cyclohexanediol, (1R,2S)-1,2-cyclohexanediol, (1S,2R)-1,2-cyclohexanediol, (1S,2S)-1,2-cyclohexanediol, (1R,2R)-1,2-diphenylethylene glycol, (1R,2S)-1,2-diphenylethylene glycol, (1S,2R)-1,2-diphenylethylene glycol, (1S,2S)-1,2-diphenylethylene glycol, 2,2′-dihydroxybiphenyl, (R)-1,1′-bi-2-naphthol, (S)-1,1′-bi-2-naphthol, (R)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1-binaphathalene)-2,2′-diol, (S)-5,5′,6,6′,7,7′,8,8′-octahydro(1,1-dinaphthalene)-2,2′-diol and the like; an optically active aminoalcohol such as (1R,2R)-1-amino-1,2-diphenylethyl alcohol, (1R,2S)-1-amino-1,2-diphenylethyl alcohol, (1S,2R)-1-amino-1,2-diphenylethyl

alcohol, (1S,2S)-1-amino-1,2-diphenylethyl alcohol and the like; an optically active diamine such as (1R,2R)-1,2-diaminocyclohexane, (1R,2S)-1,2-diaminocyclohexane, (1S,2R)-1,2-diaminocyclohexane, (1S,2S)-1,2-diaminocyclohexane, (1R,2R)-1,2-dicyclohexylethylenediamine, (1R,2S)-1,2-dicyclohexylethylenediamine, (1S,2R)-1,2-dicyclohexylethylenediamine, (1S,2S)-1,2-dicyclohexylethylenediamine, (R)-2,2'-diamino-1,1'-binaphthyl, (S)-2,2'-diamine-1,1'-binaphythyl, (1R,2R)-1,2-diphenylethylenediamine, (1R,2S)-1,2-diphenylethylenediamino, (1S,2R)-1,2-diphenylethylenediamine, (1S,2S)-1,2-diphenylethylenediamine, (1R,2R)-N-(4-toluenesulfonyl)-1,2-phenylenediamine, (1R,2S)-N-(4-toluenesulfonyl)-1,2-phenylenediamine, (1S,2R)-N-(4-toluenesulfonyl)-1,2-phenylenediamine, (1S,2S)-N-(4-toluenesulfonyl)-1,2-phenylenediamine, (1R,2R)-N,N'-di(4-toluenesulfonyl)-1,2-diphenylethylenediamine, (1R,2S)-N,N'-di(4-toluenesulfonyl)-1,2-diphenylethylenediamine, (1S,2R)-N,N'-di(4-toluenesulfonyl)-1,2-diphenylethylenediamine, (1S,2S)-N,N'-di(4-toluenesulfonyl)-1,2-diphenylethylenediamine, (R)-2,2-di(N,N'-di(4-toluenesulfonyl))aminodinaphthyl, (S)-2,2-di(N,N'-di(4-toluenesulfonyl))aminodinaphothyl and the like; and the like.

[0259]

As these compounds represented by the general formula (10), commercially available products may be used, or compounds which have appropriately prepared may be used. In addition, when for

example, diamines, aminoalcohols or mercaptoamines are used as the compound represented by the general formula (10), a diamine, an aminoalcohol, or a mercaptoamine, wherein the amino moiety is unsubstituted, is reacted with a phosphorylating agent, and then a hydrocarbon group optionally having a substituent and/or an acyl group optionally having a substituent may be introduced into the amino group, or the compound represented by the general formula (10) wherein a hydrocarbon group optionally having a substituent and/or an acyl group optionally having a substituent is/are introduced into the amino moiety may be reacted with a phosphorylating agent.

[0260]

Examples of the phosphorylating agent used upon preparation of the phosphoric acid derivative represented by the general formula (1) include a phosphorus oxyhalide such as phosphorus oxychloride, phosphorus oxybromide and the like; a phosphorus halide such as phosphorus (IV) chloride, phosphorus (IV) bromide and the like; a dihalogenophosphine such as dichloroallyloxyphosphine, dichloromethylphosphine and the like; and the like. These phosphorylating agents may be used alone, or two or more members thereof may be used in appropriate combination.

[0261]

Since the amount of each of the compound represented by the general formula (10) and the phosphorylating agent to be used is different depending on the kind of the compound represented by the general formula (10) and the phosphorylating agent to be used, they are not particularly limited, but the phosphorylating agent is appropriately selected from a range

of usually about 1.0 to 5.0 equivalent, preferably about 1.5 to 2.5 equivalent relative to the compound represented by the general formula (10) as a substrate.

[0262]

The phosphoric acid derivative may be prepared in the presence of a base, if necessary. Examples of the base include an inorganic base, an organic base and the like. Examples of the inorganic base include potassium carbonate, potassium hydroxide, lithium hydroxide, sodium hydrogen carbonate, sodium carbonate, potassium hydrogen carbonate, sodium hydroxide, magnesium carbonate, calcium carbonate and the like. Examples of the organic base include alkali metal salts/alkaline earth metal salts such as potassium naphthalenide, sodium acetate, potassium acetate, magnesium acetate, calcium acetate and the like; organic amines such as triethylamine, diisopropylethylamine, N,N-dimethylaniline, pyridine, 4-dimethylaminopyridine, 1,5-diazabicyclo[4.3.0]nona-5-ene, 1,8-diazabicyclo[5.4.0]undeca-7-ene, tri-n-butylamine, N-methylmorpholine and the like; metal hydrides such as sodium hydride, potassium hydride and the like; organic metal compounds such as methylmagnesium bromide, ethylmagnesium bromide, propylmagnesium bromide, methyllithium, ethyllithium, propyllithium, n-butyllithium, tert-butyllithium and the like; a quaternary ammonium salt; and the like.

Since the amount of the base to be used is different depending on the kind of the compound represented by the general formula (10) and the phosphorylating agent to be used, the amount is not particularly limited, but it is appropriately

selected from a range of usually 1.0 to 5.0 equivalent, preferably about 1.5 to 2.5 equivalent relative to the predicted equivalent of the generated acid.

[0263]

A phosphoric acid derivative may be prepared in the presence of a solvent, if necessary. Examples of the solvent include aliphatic hydrocarbons such as pentane, hexane, heptane, octane, decane, cyclohexane and the like; aromatic hydrocarbon such as benzene, toluene, xylene and the like; halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, carbon tetrachloride, o-dichlorobenzene and the like; ethers such as diethyl ether, diisopropyl ether, tert-butyl methyl ether, dimethoxyethane, ethylene glycol diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,3-dioxolane and the like; ketones such as acetone, methyl ethyl ketone, methyl isobutyl ketone, cyclohexanone and the like; esters such as methyl acetate, ethyl acetate, n-butylacetate, methyl propionate and the like; amides such as formamide, N,N-dimethylformamide, N,N-dimethylacetamide and the like; sulfoxides such as dimethyl sulfoxide and the like; cyano-containing organic compounds such as acetonitrile and the like; N-methylpyrrolidone and the like. These solvents may be used alone, or may be used in appropriate combination of two or more solvents.

Since the amount of the solvent to be used is different depending on the kind of the compound represented by the general formula (10) and the phosphorylating agent to be used, it is not particularly limited, but may be appropriately selected from a range of usually 0.1 to 1 M, preferably about 0.1 to 0.5 M relative to the compound represented by the general formula

(10) as a substrate.

[0264]

In the process for production of the phosphoric acid derivatives, in addition to the aforementioned base and solvent, other additives may be added, if necessary. Alternatively, a phosphoric acid derivative may be produced in a base without using a solvent.

[0265]

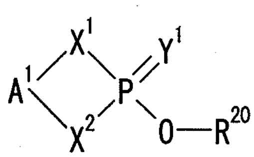
The reaction temperature is appropriately selected from a range of usually about -78 to 100°C, preferably about 0 to 50°C.

The reaction time is appropriately selected from a range of usually about 10 minutes to 10 days, preferably about 1 hour to 7 days.

[0266]

When a dihalogenoallyloxyphosphine is used as a phosphorylating agent, the phosphoric acid derivative represented by the general formula (1) can be obtained by preparing a phosphoric acid derivative represented by the general formula (9):

[0267]

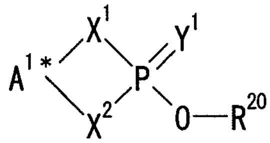


(9)

[0268]

(wherein R^{20} represents an allyl group optionally having a substituent or a benzyl group optionally having a substituent, and A^1, X^1, X^2 and Y^1 are the same as defined above), preferably an optically active phosphoric acid derivative represented by the general formula (9a):

[0269]



(9a)

[0270]

(wherein A^{1*}, X^1, X^2, Y^1 and R^{20} are the same as defined above) as an intermediate, and then reacting the obtained optically active phosphoric acid derivative represented by the general formula (9a), optionally in the presence of a transition metal catalyst and a nucleophilic agent.

Examples of the allyl group optionally having a substituent represented by R^{20} include an allyl group and a substituted allyl group.

Examples of the substituted allyl group include an allyl group in which at least one hydrogen atom of the allyl group is substituted with a substituent. The substituent may be the same as the substituent explained in the hydrocarbon group optionally having a substituent explained as a protecting group in R^1. The substituted allyl group is, for example, a substituted allyl group having 3 to 20 carbon atoms, and examples of such allyl group include croty, prenyl, methallyl, cinnamyl and the like.

Examples of the benzyl group optionally having a substituent include a benzyl group and a substituted benzyl group.

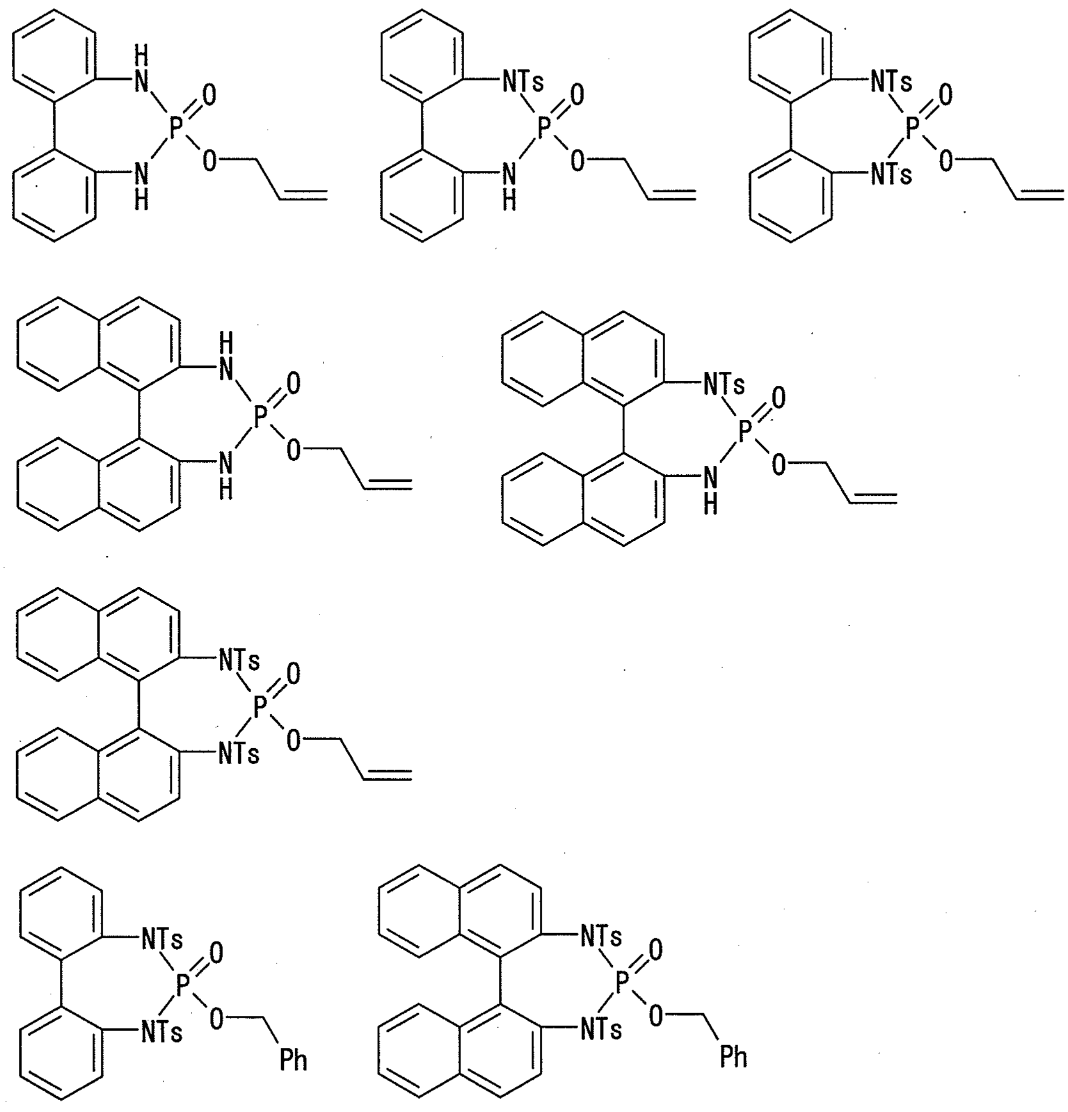
Examples of the substituted benzyl group include a benzyl group in which at least one hydrogen atom of the benzyl group is substituted with a substituent. The substituent may be the same as the substituent explained in the hydrocarbon group optionally having a substituent explained as a protecting group

in R^1. Examples of the substituted benzyl group include a substituted benzyl group having 6 to 20 carbon atoms.

[0271]

Examples of the phosphoric acid derivative represented by the general formula (9) include the following compounds:

[0272]



[0273]

Examples of the transition metal catalyst include a catalyst of a high periodic transition metal, and examples of the high periodic transition metal include palladium, platinum,

rhodium, nickel, ruthenium, molybdenum and the like.

These transition metal catalysts may be used at any oxidation state of 0 to tetravalent. In such the case, the transition metal catalyst may have various halide ions, hydroxide ion and the like as a counter anion.

In addition, these transition metal catalysts may have an appropriate ligand, if necessary. Examples of the ligand include a trivalent phosphorus ligand such as trialkylphosphine, triarylphosphine, trialkyl phosphite and the like, various heterocyclic carbene ligands, an amine ligand, a sulfur ligand and the like. These transition metal catalysts and ligands may be used alone or in appropriate combination with two or more thereof.

Since the amount of the transition metal catalyst to be used is different, depending on the kind of the compound represented by the general formula (9) and the transition metal catalyst to be used, it is not particularly limited, but is appropriately selected from a range of usually about 0.0001 to 1.0 equivalent, preferably about 0.01 to 0.1 equivalent relative to the compound represented by the general formula (9).

[0274]

Examples of the nucleophilic agent include carboxylic acids, phenols, ammonium salts, alcohols, and compounds having an active methylene moiety.

Examples of the carboxylic acids include formic acid, acetic acid, propionic acid and the like. Examples of the phenols include phenol, catechol and the like. Examples of the ammonium salts include an ammonium halide salt having at least two hydrogen atoms such as diethylammonium,

diisopropylammonium and the like. Examples of the alcohols include methanol, ethanol, 2-propanol, n-butanol, 2-ethoxyethanol, benzylalcohol and the like. Examples of the compounds having an active methylene moiety include the compound represented by the general formula (3).

As these nucleophilic agents, it may be possible to use an agent which has been prepared in advance or an agent which has been prepared by mixing an acid and a base in a reaction system.

Since the amount of the nucleophilic agent to be used is different depending on the kind of the compound represented by the general formula (9) and the transition metal catalyst to be used, it is not particularly limited, but the nucleophilic agent is appropriately selected from a range of usually about 1.0 to 10.0 equivalents, preferably about 1.2 to 2.5 equivalents relative to the compound represented by the general formula (9).

[0275]

This reaction can be performed in the presence of a base, if necessary. The kind of the base, and its amount used are the same as described above.

[0276]

Alternatively, this reaction may be performed in the presence of a solvent, if necessary. The kind of the solvents is the same as described above.

Since an amount of the solvent to be used is different depending on the kind of the compound represented by the general formula (9) and the transition metal catalyst to be used, it is not particularly limited, but is appropriately selected from a range of usually about 0.01 to 10 M, preferably about 0.1 to

0.5 M relative to the compound represented by the general formula (9).

[0277]

Since the reaction temperature is different depending on the kind of the compound represented by the general formula (9) and the transition metal catalyst to be used, it is not particularly limited, but is appropriately selected from a range of usually about 0 to 200°C, preferably about 0 to 100°C.

The reaction time is appropriately selected from a range of usually about 10 minutes to 10 days, preferably about 1 hour to 7 days.

[0278]

The phosphoric acid derivatives can be prepared optionally in an inert gas atmosphere. Examples of the inert gas include a nitrogen gas, an argon gas and the like.

[0279]

The resulting phosphoric acid derivative may be used as it is in the process of the present invention, or may be used after post-treatment, purification, isolation or the like as necessary. Examples of specific means of post-treatment, purification, isolation and the like include means known per se such as solvent extraction, liquid nature conversion, dissolution, salting out, crystallization, recrystallization, various chromatographies and the like.

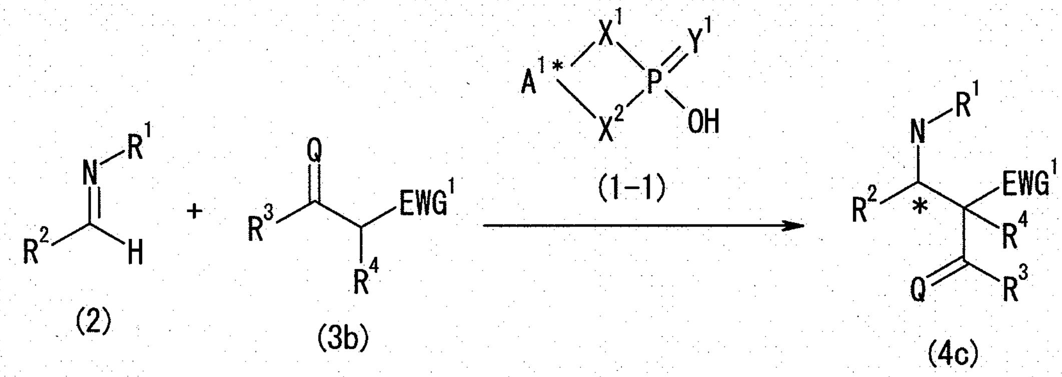
[0280]

Then, the process of the present invention will be explained using the following reaction scheme.

1) Reaction of an imine compound with a compound represented by the general formula (3):

[0281]

Scheme 1



[0282]

Scheme 1 is a reaction equation showing a reaction of obtaining optically active amines represented by the general formula (4c) as amines using an imine compound represented by the general formula (2) as the imine compound, i.e. using a compound represented by the general formula (3b) in which R^5 in the compound represented by the general formula (3) is EWG^1 as the nucleophilic compound, and using an optically active phosphoric acid derivative represented by the general formula (1-1) as the phosphoric acid derivative represented by the general formula (1).

[0283]

That is, the optically active amines represented by the general formula (4a) can be obtained by reacting an imine compound represented by the general formula (2) with a compound represented by the general formula (3b) in the presence of an optically active phosphoric acid derivative represented by the general formula (1-1).

[0284]

Since the amount of each of the imine compound represented

by the general formula (2) and the compound represented by the general formula (3b) to be used is different, depending on the kind of the imine compound represented by the general formula (2), the compound represented by the general formula (3b), and the optically active phosphoric acid derivative represented by the general formula (1-1) to be used, such amount is not particularly limited, but the compound represented by the general formula (3b) is appropriately selected from a range of usually about 0.9 to 2.0 equivalents, preferably about 1.0 to 1.5 equivalents relative to the imine compound represented by the general formula (2).

[0285]

The present process may be performed optionally in the presence of a solvent. Examples of the solvent include aliphatic hydrocarbons such as pentane, hexane, heptane, octane, decane, cyclohexane and the like; aromatic hydrocarbons such as benzene, toluene, xylene and the like; halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, deuterochloroform, carbon tetrachloride, o-dichlorobenzene and the like; ethers such as diethyl ether, diisopropyl ether, tert-butyl methyl ether, dimethoxyethane, ethylene glycol diethyl ether, tetrahydrofuran, 1,4-dioxane, 1,3-dioxolane and the like; ketones such as acetone, heavy acetone, methyl ethyl ketone, methyl isobutyl ketone, cyclohexanone and the like; tertiary alcohols such as tert-butanol and the like; esters such as methyl acetate, ethyl acetate, n-butyl acetate, methyl propionate and the like; amides such as formamide, N,N-dimethylformamide, N,N-dimethylacetamide and the like; sulfoxides such as dimethyl

sulfoxide, deuterodimethyl sulfoxide (dimethyl sulfoxide-d_6, etc.), cyano-containing organic compounds such as acetonitrile and the like; N-methylpyrrolidone; and the like. These solvents may be used alone or in appropriate combination with two or more solvents thereof.

Since the amount of a solvent when it is used is different depending on the kind of the imine compound represented by the general formula (2) and the compound represented by the general formula (3b) to be used, such amount is not particularly limited, but a substrate concentration of the imine compound represented by the general formula (2) is appropriately selected from a range of usually about 0.01 to 1 M, preferably about 0.05 to 0.2 M.

[0286]

The reaction temperature is appropriately selected from a range of usually about -78°C to 100°C, preferably about 0°C to 50°C, more preferably a range of around room temperature.

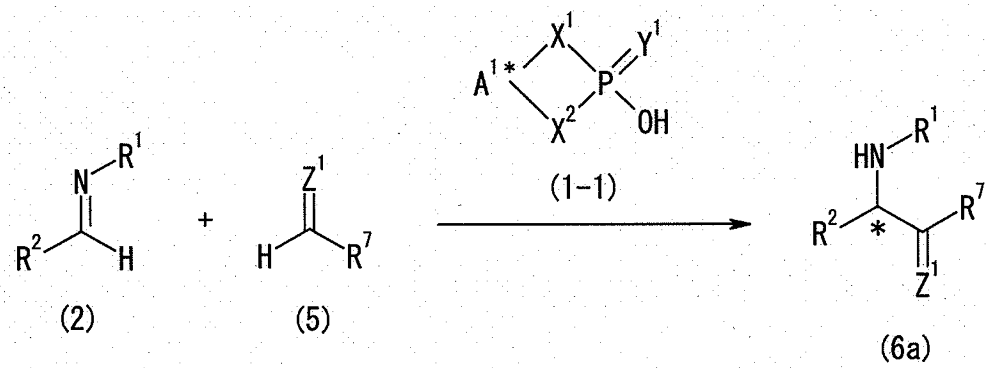
The reaction time is appropriately selected from a range of usually about 10 minutes to 10 days, preferably about 1 hour to 7 days.

[0287]

2) Reaction of an imine compound and a compound represented by the general formula (5)

[0288]

Scheme 2



[0289]

Scheme 2 is a reaction equation showing a reaction obtaining optically active amines represented by the general formula (6a) as an amine using an imine compound represented by the general formula (2) as an imine compound, using a compound represented by the general formula (5) as a nucleophilic compound, and an optically active phosphoric acid derivative represented by the general formula (1-1) as a phosphoric acid derivative represented by the general formula (1), respectively.

[0290]

That is, the optically active amines represented by the general formula (6a) can be obtained by reacting the imine compound represented by the general formula (2) with the compound represented by the general formula (5) in the presence of an optically active phosphoric acid derivative represented by the general formula (1-1).

[0291]

Since the amount of each of the imine compound represented by the general formula (2) and the compound represented by the general formula (5) to be used are different depending on the kind of the imine compound represented by the general formula (2), the compound represented by the general formula (5), and

the optically active phosphoric acid derivative represented by the general formula (1-1), such amount is not particularly limited, but the compound represented by the general formula (5) is appropriately selected from a range of usually about 0.9 to 2.5 equivalents, preferably about 1.0 to 1.5 equivalents relative to the imine compound represented by the general formula (2).

[0292]

The present process may be performed in the presence of a solvent, if necessary. Examples of the solvent include solvents exemplified in the scheme 1.

Since the amount of the solvent when it is used is different, depending on kinds of the imine compound represented by the general formula (2) and the compound represented by the general formula (5) to be used, the amount is not particularly limited, but a substrate concentration of such imine compound represented by the general formula (2) is appropriately selected from a range of usually about 0.01 to 1 M, preferably about 0.05 to 0.2 M.

[0293]

The reaction temperature is appropriately selected from a range of usually about 0°C to 100°C, preferably about 0°C to 50°C, more preferably a range of around room temperature.

The reaction time is appropriately selected from a range of usually about 10 minutes to 10 days, preferably about 1 hour to 7 days.

[0294]

The process of the present invention explained in the schemes 1 and 2 can be performed in an inert gas atmosphere.

Examples of the inert gas include a nitrogen gas, an argon gas and the like.

[0295]

The resulting optically active amines may be subjected to post-treatment, purification, isolation or the like, if necessary.

[0296]

The thus obtained amines are useful as an intermediate for drugs, agricultural chemicals or the like.

[Examples]

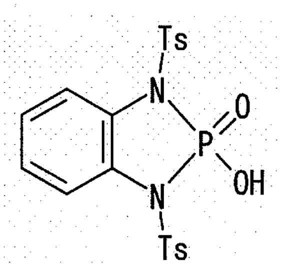
[0297]

The present invention will be explained in detail below by way of Examples and Comparative Examples, but the present invention is not limited at all by them.

[0298]

Example 1

Synthesis of the following phosphoric acid derivative 1



Phosphoric acid derivative 1

[0300]

(1) Synthesis of N,N'-di-p-toluenesulfonyl-1,2-phenylenediamine

To a solution in which 1,2-phenylenediamine (0.5 mmol) had been dissolved in pyridine (1 mL) was added p-toluenesulfonyl chloride (1.1 mmol) at room temperature, and the mixture was

reacted for 6 hours while stirring. After completion of the reaction, the reaction mixture was diluted with dichloromethane, and reverse- extracted using 1N hydrochloric acid to remove pyridine. After the organic layer was dried with anhydrous sodium sulfate, and concentrated. The resulting solid was washed using diethyl ether on a Buchner funnel, and dried under reduced pressure to obtain an objective substance as a white solid in a yield of more than 95%.

[0301]

(2) Synthesis of phosphoric acid derivative 1

Under nitrogen atmosphere, to a solution in which N,N′-di p-toluenesulfonyl-1,2-phenylenediamine (0.5 mmol) obtained in of Example 1(1) had been dissolved in pyridine (1 mL) was added dropwise phosphorus oxychloride (0.75 mmol) at room temperature. The mixture was stirred for 12 hours while stirring. After completion of the reaction, water was added, and the mixture was further stirred for 30 minutes. The resulting suspension was diluted with ethyl acetate, and reverse-extracted using 1N hydrochloric acid to remove pyridine. Purification by column chromatography in a conventional method afforded an objective substance as a white solid in more than 90% yield.

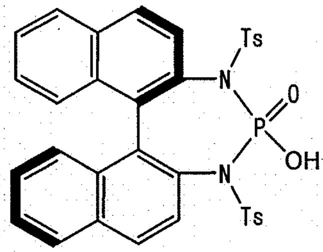
^{1}HNMR($CDCl_3$,270MHz): δ 2.30(6H,s), 6.90(2H,m), 7.22(4H,d,J=8.5Hz), 7.35(2H,m), 8.08(4H,d,J=8.5Hz).

[0302]

Example 2

Synthesis of the following optically active phosphoric acid derivative 2

[0303]



Phosphoric acid derivative 2

[0304]

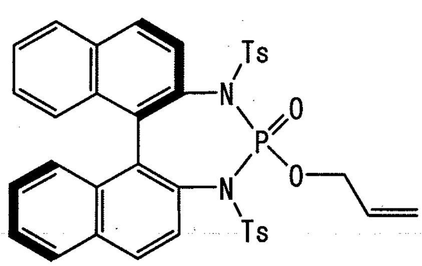
(1) Synthesis of N,N'-di-p-toluenesulfonyl-1,1'-binaphthyl-2,2'-diamine

Under nitrogen atmosphere, to a solution in which 1,1'-binaphthyl-2,2'-diamine (0.5 mmol) had been dissolved in pyridine (1 mL) was added p-toluenesulfonyl chloride (1.1 mmol) at room temperature, and the mixture was reacted for 5 to 12 hours while stirring. After completion of the reaction, the resulting red suspension was diluted with ethyl acetate, and reverse-extracted with 1N hydrochloric acid to remove pyridine. The resulting organic layer was dried with sodium sulfate to remove the solvent, and the residue was purified by column chromatography to obtain an objective substance as a pale yellow to white solid in more than 95% yield.

[0305]

(2) Synthesis of the following optically active phosphoric acid ester

[0306]



[0307]

A solution in which N,N′-di-p-toluenesulfonyl-1,1′-binaphthyl-2,2′-diamine (0.1 mmol) obtained in Example 2(1) had been dissolved in anhydrous tetrahydrofuran (5 mL) under nitrogen atmosphere was cooled to 0°C, and to this solution were added dropwise a solution of dichloroallyloxyphosphine in tetrahydrofuran (0.1 M, 2 mL, 0.2 mmol) and triethylamine (0.6 mmol). The mixture was stirred at room temperature for several hours, and cooled to 0°C again. Then, 3% aqueous hydrogen peroxide (1 mL) was added dropwise thereto to perform the reaction at 0°C for 1 to 2 hours while stirring. After completion of the reaction, the organic layer was dried, and concentrated, and the resultant solid was purified by column chromatography to obtain an objective substance as a pale yellow to white solid in more than 80% yield.

[0308]

(3) Synthesis of optically active phosphoric acid derivative 2

Optically active phosphoric acid ester (0.1 mmol) obtained in Example 2(2), triphenylphosphine (0.02 mmol) and tetrakistriphenylphosphine palladium (0.005 mmol) were mixed, and anhydrous tetrahydrofuran (1.4 mL) was added thereto under nitrogen atmosphere to obtain a solution, which was then degassed. To this solution were added triethylamine (0.3 mmol) and formic acid (0.3 mmol) at room temperature, and the mixture was made to react for 12 hours while stirring. After completion of the reaction, the resulting suspension was concentrated under reduced pressure, and the obtained solid residue was purified by column chromatography to give an objective

substance in more than 80% yield.

^{1}HNMR($CDCl_3$,270MHz): δ 1.84(6H,s), 6.24(4H,d,J=8.2Hz), 6.87(2H,d,J=8.6Hz), 7.02(2H,t,J=7.3Hz), 7.13(4H,d,J=8.2Hz), 7.32(2H,t,J=7.3Hz), 7.68(2H,d,J=8.4Hz), 7.94(2H,d,J=8.9Hz), 8.10(2H,d,J=8.4Hz).

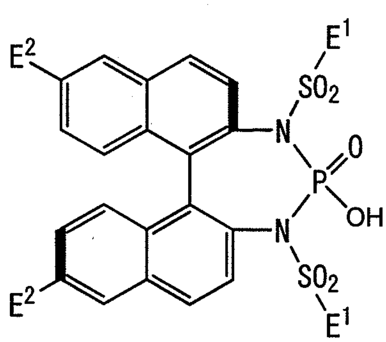
[0309]

Examples 3 to 8

Synthesis of the following optically active phosphoric acid derivatives

According to the same manner as that of Example 2 except that a sulfonyl compound shown in the following Table 1 was used in place of p-toluenesulfonyl chloride in Example 2, optically active phosphoric acid derivatives represented by the following formula were prepared.

[0310]



[0311]

Table 1

Example	Sulfonyl compound	Product	Crop/mg	Yield/%
3	CF_3SO_2Cl	E^1=CF_3 E^2=H	48.8	80
4	$PhSO_2Cl$	E^1=Ph E^2=H	59.5	95
5	β-NaphSO_2Cl	E^1=β-Naph E^2=H	67.6	93
6	p-$NO_2C_6H_4SO_2Cl$	E^1=p-$NO_2C_6H_4$ E^2=H	63.3	83
7	p-$CH_3OC_6H_4SO_2Cl$	E^1=p-$CH_3OC_6H_4$ E^2=H	67.3	98
8	3,5-$CF_3C_6H_4SO_2Cl$	E^1=3,5-$CF_3C_6H_4$ E^2=H	79.1	88
9	p-$CH_3C_6H_4SO_2Cl$	E^1=p-$CH_3C_6H_4$ E^2=Br	69.1	85

[0312]

^{1}HNMR:

Example 3: ^{1}HNMR($CDCl_3$,270MHz) δ 7.37(2H,t,J=8.2Hz), 7.45(2H,d,J=8.2Hz), 7.60(2H,t,J=8.2Hz), 7.71(2H,dd,J=1.9,8.2Hz), 7.97(4H,d,J= 8.2Hz).

Example 4: ^{1}HNMR($CDCl_3$,270MHz) δ6.49-6.55(4H,m), 6.64(2H,t,J=7.3Hz), 6.91(2H,d,J=8.1Hz), 7.05(2H,t,J=7.3Hz), 7.24-7.35(8H,m), 7.71(2H,d,J=8.1Hz), 7.90(2H,d,J=8.9Hz), 8.03(2H,d,J=8.9Hz).

Example 5: 1-(β-Naph): ^{1}HNMR(CD_3OD,270MHz) δ 6.40(2H,d,J=8.5Hz), 6.48(2H,dt, J=1.1,7.0Hz), 6.76(2H,t,J=7.0Hz), 6.94(2H,d, J=8.5Hz), 7.24(2H,dd,J=2.1,8.9Hz), 7.30(2H,d,J=7.8Hz),

7.33-7.44(8H,m), 7.67-7.70(4H,m), 8.82(2H,d,J=8.9Hz).

Example 6: : ^{1}HNMR(CD_3OD+$CDCl_3$,270MHz): δ 6.80(2H,d,J=8.0Hz), 7.11(2H,dt, J=1.4,8.0Hz), 7.28(2H,dt,J=1.4,8.0Hz), 7.31(4H,d,J=9.1Hz), 7.45(4H,d,J=9.1Hz), 7.59(2H,d,J=8.0Hz), 7.81(2H,d,J=9.1Hz), 7.85(2H,d,J=9.1Hz).

1-(p-CF_3-Ph): ^{1}HNMR(CD_3OD,270MHz): δ 6.81(4H,d,J=8.1Hz), 6.93(2H,d,J=8.6Hz), 7.18(2H,t,J=7.0Hz), δ 7.39-7.44(6H,m), 7.72-7.79(6H,m).

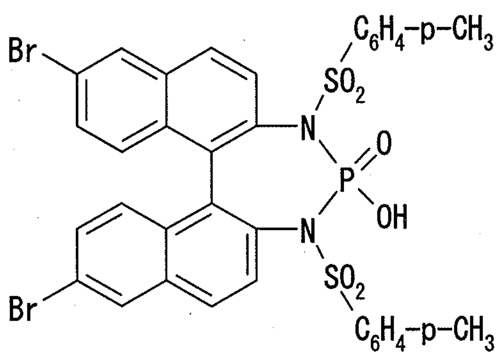
Example 7: ^{1}HNMR(CD_3OD,270MHz): δ 3.57(6H,s), 6.00(4H,d,J=8.9Hz), 6.81(2H,d,J=8.6Hz), 7.08(4H,d,J=8.9Hz), 7.11(2H,m), 7.40(2H,t, J=7.0Hz), 7.75-7.87(6H,m).

Example 8: ^{1}HNMR(CD_3OD,270MHz): δ 6.66(2H,d,J=8.0Hz), 7.05(2H,t, J=8.0Hz), 7.34(2H,t,J=8.0Hz), 7.39(2H,s), 7.70(2H,d,J=8.0Hz), 7.83(4H,s), 7.93(4H,brs).

[0313]

Example 9

Synthesis of the following optically active phosphoric acid derivative



[0315]

According to the same manner as that of Example 2 except that 6,6′-dibromo-1,1′-binaphthyl-2,2′-diamine was used in place of 1,1′-binaphthyl-2,2′-diamine in Example 2, an optically active phosphoric acid derivative represented by the

above formula was prepared. Crop: 69.1 mg. Yield: 85%.

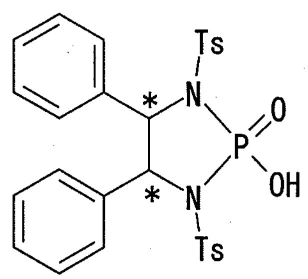
^{1}HNMR(acetone-d_6,270MHz) δ 2.01(6H,s), 6.43(4H,d,J=8.1Hz), 6.54(2H,d,J=9.0Hz), 7.07(4H,d,J=8.1Hz), 7.19(2H,d,J=9.0Hz), 7.95-8.10(6H,m).

[0316]

Example 10

Synthesis of the following optically active phosphoric acid derivative

[0317]



[0318]

According to the same manner as that of Example 2 except that (1R,2S)-diphenylethylenediamine was used in place of 1,1'-binaphthyl-2,2'-diamine in Example 2, an optically active phosphoric acid derivative represented by the above formula was prepared. Crop: 52.4 mg. Yield: 90%.

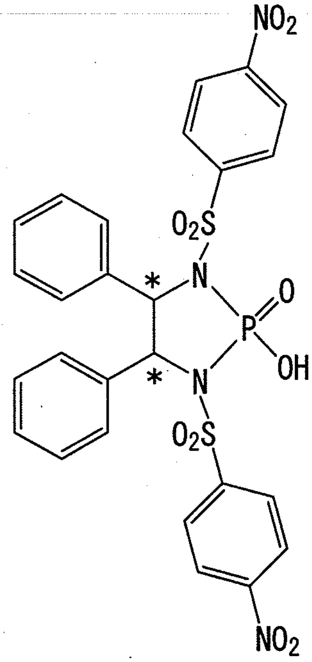
^{1}HNMR($CDCl_3$,270MHz) δ 2.23(6H,s), 4.49(2H,d,J=13.5Hz), 6.95(4H,d,J=8.1Hz), 7.04(6H,br), 7.30(4H,brd,J=7.6Hz), 7.69(4H,d,J=8.1Hz).

[0319]

Example 11

Synthesis of the following optically active phosphoric acid derivative

[0320]



[0321]

According to the same manner as that of Example 2 except that p-nitrophenylsulfonyl chloride was used in place of p-toluenesulfonyl chloride in Example 2, an optically active phosphoric acid derivative represented by the above formula was prepared. Crop: 51.6 mg. Yield: 90%.

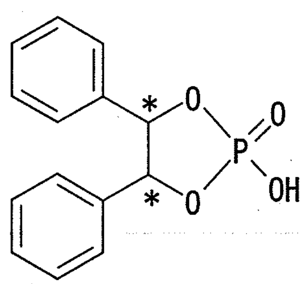
^{1}HNMR($CDCl_3$,270MHz) δ 4.48(2H,d,J=13.2Hz), 6.96(6H,t, J=3.2Hz), 7.44(4H,m), 7.89-7.96(8H,m).

[0322]

Example 12

Synthesis of the following optically active phosphoric acid derivative

[0323]



[0324]

According to the same manner as that of Example 1(2) except that (1R,2S)-diphenylethylene glycol was used in place of N,N'-di-p-toluenesulfonyl-1,2-phenylenediamine in Example 1(2), an optically active phosphoric acid derivative represented by the above formula was prepared.

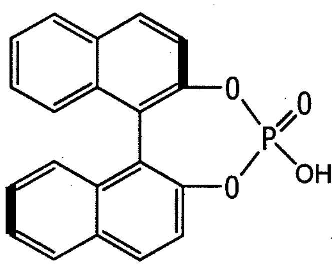
^{1}HNMR(CD_3OD,270MHz) δ 5.30(2H,br), 7.14(4H,br), 7.27(2H,br), 7.37(4H,br).

[0325]

Example 13

Synthesis of the following optically active phosphoric acid derivative

[0326]



[0327]

According to the same manner as that of of Example 1(2) except that 1,1'-binaphthyl-2,2'-diol was used in place of 1,1'-binaphthyl-2,2'-diamine in Example 1(2), an optically active phosphoric acid derivative represented by the above formula was prepared.

[0328]

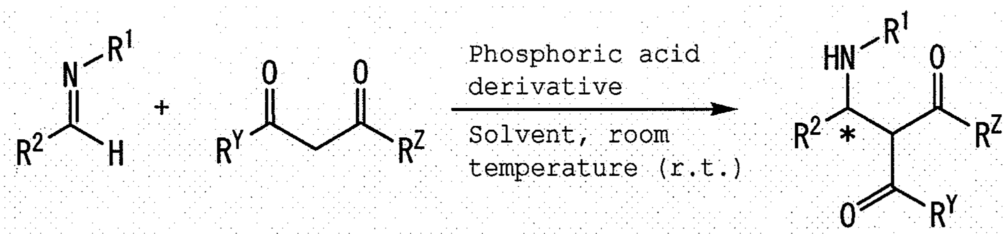
Example 14

Synthesis of optically active amines

Under nitrogen atmosphere, to a solution in which 0.002 mmol of the following phosphoric acid derivative and 0.1 mmol

of each of various imine compounds had been dissolved in 800 μL of a solvent was added 0.11 mmol of acetylacetones at room temperature to perform the reaction while stirring. After completion of the reaction, reaction completion was confirmed by NMR, and the reaction solution was purified by silica gel column chromatography to obtain an objective substance. The optically active phosphoric acid derivative, the imine compound, the reaction time, the crop and the yield used are shown in the following Tables 2 to 7.

[0329]



[0330]

[Table 2]

Entry	R^2	R^1	R^Y, R^Z	Phosphoric acid derivative	Solvent	Reaction time	Yield (%)	Optical yield (%)
1	Ph	Bz	Me	achiral	$CDCl_3$	10 min	91	-
2	Ph	Bz	Me	1:R= Tf	$CDCl_3$	2.5d	68	14 (f)
3	Ph	Bz	Me	1:R= Ph	$CDCl_3$	6d	50	3 (s)
4	Ph	Bz	Me	1:R= β-Naph	$CDCl_3$	6d	69	32 (s)
5	Ph	Bz	Me	1:R= 4-MeOPh	$CDCl_3$	6d	68	11 (s)
6	Ph	Bz	Me	1:R= Ts	$CDCl_3$	6d	50	41 (f)
7	Ph	Bz	Me	1:R= 4-CF_3Ph	$CDCl_3$	2.5d	63	4 (s)
8	Ph	Bz	Me	1:R= 4-NO_2Ph	$CDCl_3$	3d	51	28 (s)
9	Ph	Bz	Me	1:R= 3,5-CF_3Ph	$CDCl_3$	2.5d	66	5 (f)

10	Ph	Bz	Me	1:R= Ts, 6,6'-Br-	$CDCl_3$	4d	59	10 (s)
11	Ph	Bz	Me	2:R= H	$CDCl_3$	2h	92	20 (s)
12	Ph	Bz	Me	2:R= Ph	$CDCl_3$	3d	73	31 (s)
13	Ph	Bz	Me	2:R= β-Naph	$CDCl_3$	2d	74	40 (s)
14	Ph	Bz	Me	2:R= 4-MeOPh	$CDCl_3$	5d	72	21 (s)
15	Ph	Bz	Me	2:R= 4-MePh	$CDCl_3$	4.5d	70	51 (s)
16	Ph	Bz	Me	2:R= 4-t-BuPh	$CDCl_3$	3.5d	79	23 (s)
17	Ph	Bz	Me	2:R= 4-PhPh	$CDCl_3$	3.5d	81	43 (s)
18	Ph	Bz	Me	2:R= 4-CF_3Ph	$CDCl_3$	5.5d	77	66 (s)
19	Ph	Bz	Me	2:R= 4-NO_2Ph	$CDCl_3$	4d	82	14 (s)
20	Ph	Bz	Me	2:R= 3,4,5-F_3Ph	$CDCl_3$	14h	81	7 (s)
21	Ph	Bz	Me	2:R= 3,5-PhPh	$CDCl_3$	1.5d	80	3 (s)
22	Ph	Bz	Me	2:R=3,5-CF_3Ph	$CDCl_3$	14h	81	3 (s)
23	Ph	Bz	Me	2:R= OMe	$CDCl_3$	5d	70	31 (f)
24	Ph	Bz	Me	2:R= Br	$CDCl_3$	6h	99	61 (s)
25	Ph	Bz	Me	2:R= I	$CDCl_3$	3d	57	21 (s)

[0331]

[Table 3]

Entry	R^2	R^1	R^Y, R^Z	Phosphoric acid derivative	Solvent	Reaction time	Yield (%)	Optical yield (%)
26	Ph	Bz	Me	2:R=TPS	$CDCl_3$	7d	79	5 (s)
27	Ph	Bz	Me	2:R=H, 6,6'-Br-	$CDCl_3$	5d	71	20 (s)
28	Ph	Bz	Me	3:R= Ts	$CDCl_3$	2d	83	15 (f)
29	Ph	Bz	Me	3:R=4-NO_2-Ph	$CDCl_3$	5d	76	4 (s)
30	Ph	Bz	Me	4:R = Ts	$CDCl_3$	1d	87	5 (s)

31	Ph	Bz	Me	5	$CDCl_3$	2h	75	3 (f)
32	Ph	Bz	R^Y= Ph, R^Z= H	achiral	$CDCl_3$	10 min	87	-
33	Ph	Bz	R^Y, R^Z= $-(CH_2)_3-$	achiral	$CDCl_3$	10 min	83	-
34	Ph	Bz	R^Y, R^Z = Ph	achiral	$CDCl_3$	10 min	89	-
35	Ph	Bz	R^Y = OMe, R^Z = Me	achiral	$CDCl_3$	4h	93	-
36	Ph	Bz	R^Y = NMe_2, R^Z = Me	achiral	$CDCl_3$	10 min	94	-
37	Ph	1-Naphthoyl	Me	achiral	$CDCl_3$	20 min	90	-
38	Ph	1-Naphthoyl	Me	1:R= β-NaphSO_2	$CDCl_3$	2.5d	82	11 (s)
39	Ph	1-Naphthoyl	Me	1:R=Ts	$CDCl_3$	2.5d	82	33 (s)
40	Ph	1-Naphthoyl	Me	2:R=H	$CDCl_3$	20 min	88	17 (s)
41	Ph	1-Naphthoyl	Me	2:R=Ph	$CDCl_3$	3d	79	21 (s)
42	1-Naphthyl	Bz	Me	achiral	$CDCl_3$	20 min	95	-
43	1-Naphthyl	Bz	Me	1:R=Ts	$CDCl_3$	4d	80	14 (f)
44	Ph	Boc	Me	achiral	$CDCl_3$	10 min	95	-

[0332]

[Table 4]

Entry	R^2	R^1	R^Y, R^Z	Phosphoric acid derivative	Solvent	Reaction time	Yield (%)	Optical yield (%)
51	Ph	Boc	Me	2:R=H	Ether	2.5d	58	37 (S)
52	Ph	Boc	Me	2:R=H	THF	2.5d	63	31 (R)
53	Ph	Boc	Me	2:R=H	$CDCl_3$	1.5h	90	51 (S)
54	Ph	Boc	Me	2:R=H	$CDCl_3$	17h	87	28 (S)
55	Ph	Boc	Me	2:R=H	$CDCl_3$	<4h	93	81 (S)
56	Ph	Boc	Me	2:R=H	$CDCl_3$	5h	89	19 (R)
57	Ph	Boc	Me	2:R=H	$CDCl_3$	1.5h	92	91 (S)
58	Ph	Boc	Me	2:R=H	toluene	2h	85	82 (S)
59	Ph	Boc	Me	2:R=H	CH_2Cl_2	2h	88	90 (S)
60	Ph	Boc	Me	2:R=H	$^iPr_2O$	2h	91	85 (S)
61	Ph	Boc	Me	2:R=H	ether	2h	90	83 (S)
62	Ph	Boc	Me	2:R=H	MeCN	2h	78	40 (S)
63	Ph	Boc	Me	2:R=H	THF	2h	30	19 (S)
64	Ph	Boc	Me	2:R=4-(2-Naph)-Ph	$CDCl_3$	10 min	98	93 (S)
65	Ph	Boc	Me	2:R=4-(2-Naph)-Ph	toluene	1h	94	86 (S)
67	Ph	Boc	Me	2:R=4-(2-Naph)-Ph	CH_2Cl_2	1h	99	95 (S)
68	Ph	Boc	Me	2:R=4-(2-Naph)-Ph	ether	1h	92	94 (S)*
69	4-MeO-C6H4-	Boc	Me	2:R=4-(2-Naph)-Ph	CH_2Cl_2	1h	92	86 (S)
70	4	Boc	Me	achiral	$CDCl_3$	10min	97	-

71	4	Boc	Me	2:R=4-(2-Naph)-Ph	CH_2Cl_2	1h	93	90
72	4	Boc	Me	achiral	$CDCl_3$	10 min	92	-

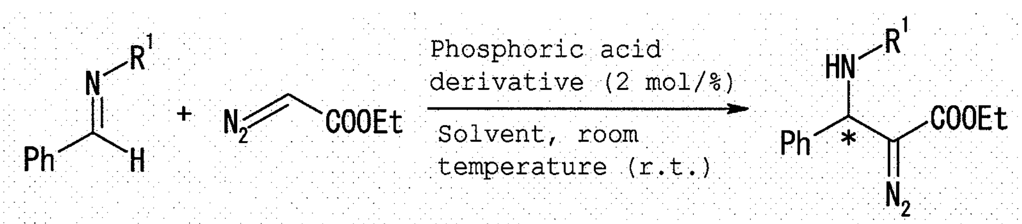
[0333]

[Table 5]

Entry	R^2	R^1	RY, RZ	Phosphoric acid derivative	Solvent	Reaction time	Yield (%)	Optical yield (%)
76	4-Br-C_6H_4-	Boc	Me	achiral	$CDCl_3$	30 min	96	-
77	4-Me-C_6H_4-	Boc	Me	2:R=4-(2-Naph)-Ph	CH_2Cl_2	1h	94	93
78	2-Me-C_6H_4-	Boc	Me	achiral	$CDCl_3$	20 min	96	-
79	1-Naphthyl-	Boc	Me	2:R=4-(2-Naph)-Ph	CH_2Cl_2	1h	99	92
80	1-Naphthyl-	Boc	Me	achiral	$CDCl_3$	20 min	99	-
81	Ph	Boc	Me	2:R=4-CF_3Ph	$CDCl_3$	1.5h	90	69 (S)
82	Ph	Boc	Me	2:R=4-NO_2Ph	$CDCl_3$	1h	92	69 (S)
83	Ph	Boc	Me	2:R=(3,4,5-F_3Ph)	$CDCl_3$	0.5h	88	36 (S)
84	Ph	Boc	Me	2:R=(3,5-PhPh)	$CDCl_3$	0.5h	87	45 (R)
85	Ph	Boc	Me	2:R=(3,5-CF_3Ph)	$CDCl_3$	1h	90	22 (R)

86	Ph	Boc	Me	2:R=OMe	$CDCl_3$	2d	84	10 (S)
87	Ph	Boc	Me	2:R=Br	$CDCl_3$	1h	91	>34 (R)
88	Ph	Boc	Me	2:R=I	$CDCl_3$	2d	89	31 (S)
89	Ph	Boc	Me	2:R=TPS	$CDCl_3$	2.5d	90	
90	Ph	Boc	Me	2:R=H, 6,6′-Br-	$CDCl_3$	1d	84	
91	Ph	Boc	R^Y=OMe, R^Z=Me	Achiral	$CDCl_3$	4h	92	
92	Ph	Boc	R^Y=NMe_2, R^Z=Me	achiral	$CDCl_3$	10min	96	

[0334]



[0335]

[Table 6]

Entry	R^1	Phosphoric acid derivative	Solvent	Reaction time	Yield (%)	Optical yield (%)
1	Bz	achiral	toluene	1h	27	rac
2	Bz	1:R=Ts	$CDCl_3$	7d	61	22 (f)
3	Bz	1:R=Naph	$CDCl_3$	6d	58	22 (s)
4	Bz	2:R=H	$CDCl_3$	10 min	59	5 (f)
5	Bz	2:R=Ph	$CDCl_3$	5d	40	23 (f)
6	Bz	2:R=p-MeO-Ph	$CDCl_3$	7d	57	9 (f)
7	Bz	2:R=p-Me-Ph	$CDCl_3$	4.5d	42	22 (f)
8	Bz	2:R=p-t-Bu-Ph	$CDCl_3$	3.5d	54	5 (f)
9	Bz	2:R=p-Ph-Ph	$CDCl_3$	3.5d	62	30 (f)
10	Bz	2:R=p-CF_3-Ph	$CDCl_3$	3.5d	70	22 (f)

11	Bz	2:R=p-NO_2-Ph	$CDCl_3$	7d	48	16 (f)
12	Bz	2:R=3,4,5-F_3-Ph	$CDCl_3$	4d	52	10 (f)
13	Bz	2:R=3,5-Me-Ph	$CDCl_3$	4d	47	33 (f)
14	Bz	2:R=3,5-Ph-Ph	$CDCl_3$	3d	53	50 (f)
15	Bz	2:R=3,5-CF_3-Ph	$CDCl_3$	6d	60	38 (f)
16	Bz	2:R=3,5-CF_3-Ph	ether	2d	58	32 (f)
17	Bz	2:R=3,5-CF_3-Ph	THF	2d	39	27 (f)
18	Bz	2:R=β-Naph	$CDCl_3$	4d	58	28 (f)
19	Bz	2:R=Br	$CDCl_3$	5d	46	31 (f)
20	Bz	2:R=I	$CDCl_3$	7d	43	26 (f)
21	Bz	2:R=OMe	$CDCl_3$	8d	50	10 (f)
22	Bz	2:R=TPS	$CDCl_3$	11d	52	3 (f)
23	Bz	2:R=$Ph_2C(OH)$	$CDCl_3$	4d	61	51 (s)
24	Bz	2:R=$Ph_2C(OH)$	toluene	3d	31	11 (s)
25	Bz	2:R=$Ph_2C(OH)$	THF	3d	25	18 (s)

[0336]

[Table 7]

Entry	R^1	Phosphoric acid derivative	Solvent	Reaction time	Yield (%)	Optical yield (%)
26	Bz	2:R=H, 6,6′-Br-	$CDCl_3$	7d	46	7 (s)
27	α-Naph	achiral	toluene	1h	30	rac
28	α-Naph	2:R=3,5-t-Bu-Ph	$CDCl_3$	3d	68	58 (s)
29	α-Naph	2:R=3,5-Ph-Ph	$CDCl_3$	4.5d	68	70 (s)
30	α-Naph	2:R=$Ph_2C(OH)$	$CDCl_3$	4.5d	52	72 (f)
31	β-naph	achiral	toluene	1h	34	rac
32	β-Naph	2:R=3,5-Ph-Ph	$CDCl_3$	3d	52	48 (s)
33	Boc	achiral	$CDCl_3$	10 min	37	rac
34	Boc	2:R=H	$CDCl_3$	10 min	90	8 (f)
35	Boc	2:R=Ph	$CDCl_3$	5d	46	14 (f)

36	Boc	2:R=p-MeO-Ph	$CDCl_3$	6d	40	2 (s)
37	Boc	2:R=p-Me-Ph	$CDCl_3$	4d	46	13 (f)
38	Boc	2:R=p-t-Bu-Ph	$CDCl_3$	3d	48	36 (f)
39	Boc	2:R=p-Ph-Ph	$CDCl_3$	4h	60	8 (f)
40	Boc	2:R=p-CF_3-Ph	$CDCl_3$	3d	44	12 (f)
41	Boc	2:R=p-NO_2-Ph	$CDCl_3$	6d	31	2 (f)
42	Boc	2:R=3,4,5-F3-Ph	$CDCl_3$	4d	51	9 (f)
43	Boc	2:R=3,5-Ph-Ph	$CDCl_3$	1d	67	8 (f)
44	Boc	2:R=3,5-CF_3-Ph	$CDCl_3$	3d	50	9 (s)
45	Boc	2:R=β-Naph	$CDCl_3$	2d	49	8 (f)
46	Boc	2:R=Br	$CDCl_3$	6d	48	26 (f)
47	Boc	2:R=I	$CDCl_3$	3d	59	18 (f)
48	Boc	2:R=H 6,6′-Br-	$CDCl_3$	7d	37	20 (s)

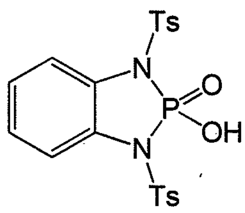
[0337]

In the reaction in the above Table, min represents minute, h represents hour, and d represents day, respectively.

Additionally, in the above Table, ether represents diethyl ether, $^{i}Pr_2O$ represents diidopropyl ether, MeCN represents acetonitrile, THF represents tetrahydrofuran, Tf represents trifluoromethyl, and TPS represents triphenylsilyl, respectively.

Phosphoric acid derivative:

[0338]



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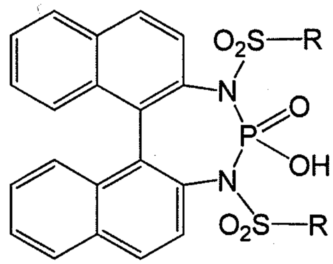

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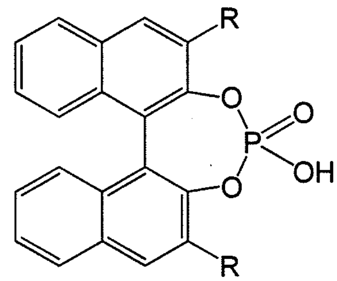
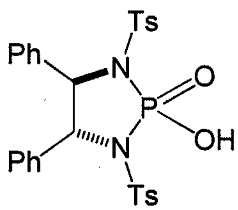


2



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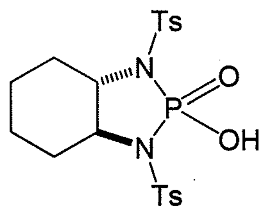
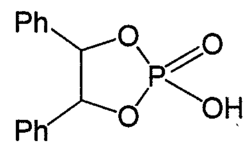


4

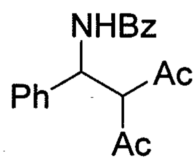


5

[0339]

NMR data and melting points of products:

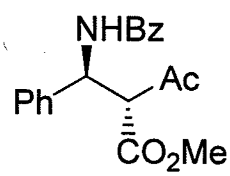
[0340]



[0341]

^{1}H NMR ($CDCl_3$,270MHz): δ 2.10(3H,s), 2.30(3H,s), 4.90(1H,d, J=5.1Hz), 6.04(1H,dd,J=5.1,9.2Hz), 7.20-7.30(1H,m), 7.31 (4H,d,J=4.1Hz), 7.41(2H,tt,J=1.6,7.3Hz), 7.50(1H,tt,J= 1.6,7.3Hz), 7.78(2H,dt,J=1.6,7.3Hz), 7.93(1H,brd,J=9.2Hz). Melting point; 193-194°C.

[0342]

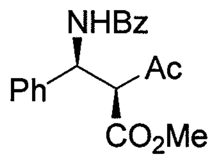


[0343]

major isomer: ^{1}H NMR ($CDCl_3$,270MHz): δ 2.38(3H, s), 3.66(3H,s),

4.15(1H,d,J=3.8Hz), 6.09(1H,dd,J=3.8,9.5Hz), 7.22-7.33(5H,m), 7.39-7.54(3H,m), 7.78-7.83(2H,m), 8.14(1H,brd,J=9.5Hz). Melting point (diastero-mixture); 158°C.

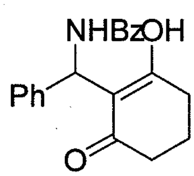
[0344]



[0345]

minor isomer: ^{1}H NMR ($CDCl_3$,270MHz): δ 2.15(3H,s), 3.70(3H,s), 4.20(1H,d,J=4.9Hz), 5.94(1H,dd,J=4.9,8.6Hz), 7.22-7.33(5H,m), 7.39-7.54(3H,m), 7.78-7.83(2H,m), 7.87(1H,brd,J=8.6Hz). Melting point (diastero-mixture); 158°C.

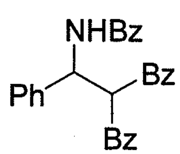
[0346]



[0347]

^{1}H NMR ($CDCl_3$,270MHz): δ 1.95(2H,brquin,J=6.5 Hz), 2.33 (2H,brt,J=6.5Hz), 2.64(2H,brt,J=6.5Hz), 6.59(1H,d, J=9.5Hz), 7.16-7.29(3H,m), 7.38-7.55(5H,m), 7.87(2H,d,J=8.4Hz), 8.93 (1H,brd,J=9.5Hz), 11.27(1H,br). Melting point; 208-209°C.

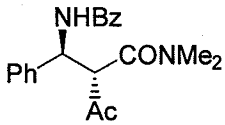
[0348]



[0349]

^{1}H NMR ($CDCl_3$,270MHz): δ 6.08(1H,dd,J=3.2,8.1Hz), 6.10(1H,s), 7.17-7.56(13H,m), 7.64(1H,td,J=1.4,7.3Hz), 7.79(2H,td, J=1.4,8.1Hz), 7.84(2H,td,J=1.4,6.5Hz), 8.06(2H,td,J=1.6, 7.3Hz), 8.52(1H,d,J=8.1Hz). Melting point; 222°C.

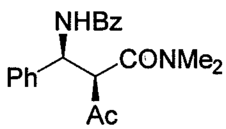
[0350]



[0351]

major isomer: [1]H NMR ($CDCl_3$,270MHz): δ 2.16(3H,s), 2.80(3H,s), 3.01(3H,s), 4.34(1H,d,J=7.3Hz), 5.90(1H,dd,J=7.0,9.2Hz), 7.14-7.46(8H,m), 7.82(2H,td,J=1.6,7.0Hz), amide proton was not detected. Melting point (diastereo-mixture); 69-71°C.

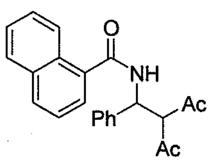
[0352]



[0353]

minor isomer: [1]H NMR ($CDCl_3$,270MHz): δ 2.29(3H,s), 2.59(3H,s), 2.84(3H,s), 4.11(1H,d,J=3.2Hz), 5.97(1H,dd,J=3.2,8.1Hz), 7.14-7.46(8H,m), 7.82(2H,td,J=1.6,6.8Hz), 9.13(1H,brd, J=8.1Hz). Melting point (diastero-mixture); 69-71°C.

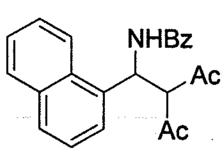
[0354]



[0355]

[1]H NMR ($CDCl_3$,270MHz): δ 2.13(3H,s), 2.38(3H,s), 4.42(1H,d, J=5.4Hz), 6.17(1H,dd,J=5.4,9.5Hz), 7.24-7.36(5H,m), 7.42 (1H,d,J=7.3Hz), 7.44-7.53(2H,m), 7.55(1H,br), 7.59(1H,dd, J=1.4,7.0Hz), 7.84(1H,m), 7.91(1H,d,J=8.1Hz), 8.21(1H,m).

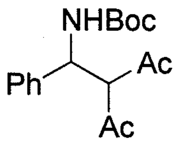
[0356]



[0357]

^{1}H NMR ($CDCl_3$,270MHz): δ 1.95(3H,s), 2.45(3H,s), 4.53(1H,d, J=4.3Hz), 6.81(1H,dd,J=4.3,8.9Hz), 7.36-7.56(6H,m), 7.64 (1H,dt,J=1.4,7.0Hz), 7.60-7.85(3H,m), 7.89(1H,d,J=8.6Hz), 8.21(1H,d,J=8.6Hz).

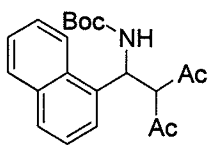
[0358]



[0359]

^{1}H NMR ($CDCl_3$,270MHz): δ 1.37(9H,s), 2.09(3H,s), 2.17(3H,brs), 4.18(1H,d,J=6.8Hz), 5.46(1H,br), 5.73(1H,br), 7.20-7.34 (5H,m). Melting point; 176°C.

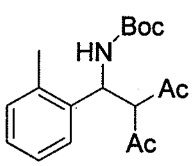
[0360]



[0361]

^{1}H NMR ($CDCl_3$,270MHz): δ 1.37(9H,s), 1.96(3H,s), 2.30(3H,s), 4.40(1H,d,J=5.4Hz), 6.16(1H,brs), 6.29(1H,brs), 7.37-7.44 (2H,m), 7.50(1H,t,J=6.8Hz), 7.59(1H,dt,J=1.4,6.8Hz) 7.70-7.80(1H,m), 7.86(1H,d,J=7.8Hz) 8.16(1H,d,J=8.4Hz).

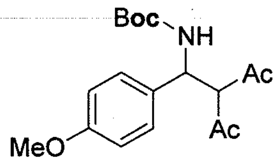
[0362]



[0363]

^{1}H NMR ($CDCl_3$,270MHz): δ 1.35(9H,s), 2.11(6H,s), 2.48(3H,s), 4.11(1H,d,J=7.0Hz), 5.66(2H,brs), 7.13-7.16(4H,m).

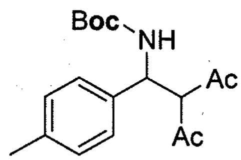
[0364]



[0365]

^{1}H NMR ($CDCl_3$,270MHz): δ 1.39(9H,s), 2.10(3H,s), 2.12 (3H,s), 3.75(3H,s), 4.15(1H,d,J=7.0Hz), 5.40(1H,brs), 5.65(1H,brs), 6.81(2H,d,J=8.5Hz), 7.16(2H,d,J=8.5Hz).

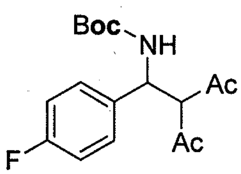
[0366]



[0367]

^{1}H NMR ($CDCl_3$,270MHz): δ 1.36(9H,s), 2.10(3H,s), 2.15(3H,s), 2.28(1H,d,J=5.4Hz), 4.17(1H,d,J=7.0Hz), 5.43(1H,brs), 5.70 (1H,brs), 7.07-7.15(4H,m).

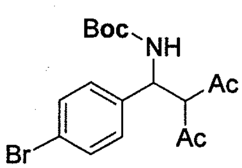
[0368]



[0369]

^{1}H NMR ($CDCl_3$,270MHz): δ 1.36(9H,s), 2.09(3H,s), 2.16(3H,s), 4.15(1H,d,J=6.8Hz), 5.42(1H,brs), 5.47(1H,brs), 6.94-7.03 (2H,m), 7.19-7.26(2H,m).

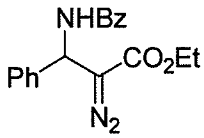
[0370]



[0371]

^{1}H NMR ($CDCl_3$,270MHz): δ 1.37(9H,s), 2.08(3H,s), 2.19(3H,s), 4.14(1H,d,J=6.2Hz), 5.41(1H,brs), 5.79(1H,brs), 7.14(2H,d, J=8.5Hz), 7.42(2H,d,J=8.5Hz).

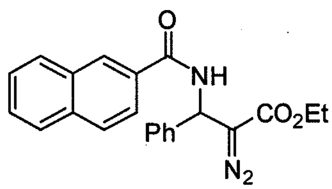
[0372]



[0373]

^{1}H NMR ($CDCl_3$,270MHz): δ 1.27(3H,t,J=7.0Hz), 4.25(2H,q, J=7.0Hz), 6.20(1H,d,J=8.4Hz), 7.28-7.56(9H,m), 7.84 (2H,d, J=5.9Hz).

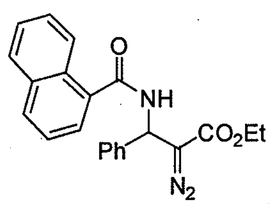
[0374]



[0375]

^{1}H NMR ($CDCl_3$,270MHz): δ 1.28(3H,t,J=7.0Hz), 4.27(2H,q, J=7.0Hz), 6.27(1H,d,J=8.1Hz), 7.33-7.61(8H,m), 7.87-7.96 (4H,m), 8.36(1H,s).

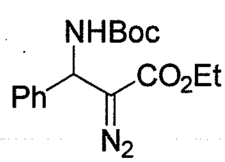
[0376]



[0377]

^{1}H NMR ($CDCl_3$,270MHz): δ 1.28(3H,t,J=7.0Hz), 4.26(2H,q, J=7.0Hz), 6.30(1H,d,J=7.8Hz), 7.30-7.58(9H,m), 7.68(1H,d, J=7.0Hz), 7.87-7.96(2H,m), 8.37(1H,d,J=9.4Hz).

[0378]



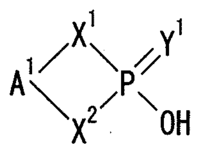
[0379]

^1H NMR ($CDCl_3$,270MHz): δ 1.25(3H,t,J=7.0Hz), 1.45(9H,s), 4.22(2H,q,J=7.0Hz), 5.39(1H,brs), 5.39(1H,d,J=7.6Hz), 7.25-7.41(5H,m).

[Document Name] CLAIMS

[Claim 1]

A process for preparing an amine, comprising reacting an imine compound and a nucleophilic compound (provided that trialkylsilyl vinyl ethers are excluded) in the presence of a phosphoric acid derivative represented by the general formula (1):



(1)

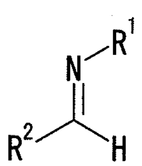
(wherein A^1 represents a spacer; X^1 and X^2 each independently represent a divalent nonmetal atom or a divalent nonmetal atomic group; and Y^1 represents an oxygen atom or a sulfur atom).

[Claim 2]

The process according to claim 1, wherein the phosphoric acid derivative represented by the general formula (1) is an optically active phosphoric acid derivative, and the obtained amine is an optically active amine.

[Claim 3]

The process according to claim 1, wherein the imine compound is an imine compound represented by the general formula (2):



(2)

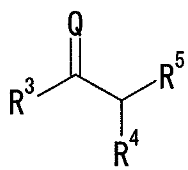
(wherein R^1 represents a hydrogen atom or a protecting group, and R^2 represents a group having no α-proton or represents an

unsaturated hydrocarbon group).

[Claim 4]

The process according to claim 1, wherein the nucleophilic compound is

a compound represented by the general formula (3):



(3)

(wherein

R^3 represents a hydrogen atom, a hydrocarbon group optionally having a substituent, a heterocyclic group optionally having a substituent, an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent, an aralkyloxy group optionally having a substituent or a substituted amino group;

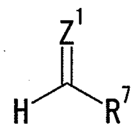
R^4 and R^5 each independently represent a hydrogen atom, a hydrocarbon group optionally having a substituent, a heterocyclic group optionally having a substituent, EWG^1 (EWG^1 represents an electron withdrawing group), an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent, an aralkyloxy group optionally having a substituent, an alkylthio group optionally having a substituent, an arylthio group optionally having a substituent, an aralkylthio group optionally having a substituent or a hydroxy group;

Q represents a group giving a tautomer of a compound represented by the general formula (3); or

R^3 and R^4, R^3 and R^5, or R^4 and R^5 may be taken together to

form a ring);

a compound represented by the general formula (5):



(5)

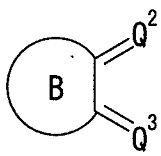
(wherein

R^7 represents a hydrogen atom, a hydrocarbon group optionally having a substituent, a heterocyclic group optionally having a substituent, an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent or an aralkyloxy group optionally having a substituent, an alkylthio group optionally having a substituent, an arylthio group optionally having a substituent, an aralkylthio group optionally having a substituent or EWG^2 (EWG^2 represents an electron withdrawing group), and

Z^1 represents N_2, $P(R^8)_3$ (three R^8s are the same or different, and represent a hydrogen atom, a hydrocarbon group optionally having a substituent, a heterocyclic group optionally having a substituent, an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent or an aralkyloxy group optionally having a substituent) or CR^9R^{10} (R^9 and R^{10} each independently represent a hydrogen atom, a hydrocarbon group optionally having a substituent, a heterocyclic group optionally having a substituent, an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent, an aralkyloxy group optionally having a substituent, an alkylthio group optionally having a substituent, an arylthio group optionally having a substituent, an aralkylthio group optionally having a substituent, an amino group or a substituted amino group, provided that either one

of R^9 and R^{10} represents an alkoxy group optionally having a substituent, an aryloxy group optionally having a substituent, an aralkyloxy group optionally having a substituent, an alkylthio group optionally having a substituent, an arylthio group optionally having a substituent, an aralkylthio group optionally having a substituent, an amino group or a substituted amino group)); or

a compound represented by the general formula (7):



(7)

(wherein

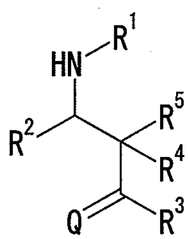
ring B represents an aliphatic ring or an aliphatic heterocycle, and

Q^2 and Q^3 each independently represent an oxygen atom, NR^{17} (R^{17} represents a hydrogen atom or a protecting group) or a sulfur atom).

[Claim 5]

The process according to claim 1, wherein the obtained amine is

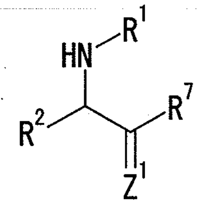
an amine represented by general formula (4):



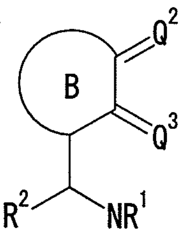
(4)

(wherein R^1 to R^5 and Q are the same as defined above);

an amine represented by the general formula (6):

 (6)

(wherein R^1, R^2, R^7 and Z^1 are the same as defined above); or an amine represented by the general formula (8):

 (8)

(wherein R^1, R^2, Q^2 and Q^3 are the same as defined above).

[Claim 6]

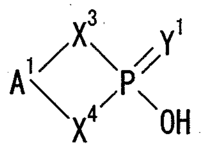
The process according to claim 5, wherein the amine represented by the general formula (4), (6), or (8) is an optically active amine.

[Claim 7]

The process according to claim 1, wherein the divalent nonmetal atom or the divalent nonmetal atomic group represented by X^1 and X^2 in the general formula (1) is an oxygen atom, $-NR^{13}-$ (R^{13} represents a hydrogen atom, a hydrocarbon group optionally having a substituent or an acyl group optionally having a substituent), a sulfur atom or $-CR^{15}R^{16}-$ {R^{15} and R^{16} each independently represent a hydrogen atom, a hydrocarbon group optionally having a substituent or EWG^3 (EWG^3 represents an electron withdrawing group), provided that either one of R^{15} and R^{16} is EWG^3}.

[Claim 8]

A phosphoric acid derivative represented by the general formula (1a):



(1a)

(wherein

A^1 represents a spacer;

X^3 and X^4 each independently represent an oxygen atom, $-NR^{13}-$ (R^{13} represents a hydrogen atom, a hydrocarbon group optionally having a substituent or an acyl group optionally having a substituent), a sulfur atom or $-CR^{15}R^{16}$ {R^{15} and R^{16} each independently represent a hydrogen atom, a hydrocarbon group optionally having a substituent or EWG^3 (EWG^3 represents an electron withdrawing group), provided that either one of R^{15} and R^{16} is EWG^3}; and

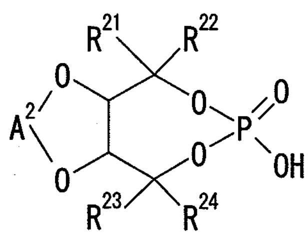
Y^1 represents an oxygen atom or a sulfur atom, provided that when i) X^3=X^4, then X^3 and X^4 are each $-NR^{13}-$ (R^{13} is a hydrogen atom, a hydrocarbon group optionally having a substiuent or an acyl group optionally having a substituent), a sulfur atom or $-CR^{15}R^{16}-$, or when X^3 and X^4 are each $-NR^{13}-$, then the $-NR^{13}-$ is $-NR^a-$ (R^a represents an acyl group derived from sulfonic acid), or when ii) X^3 and X^4 are different from each other, then either one of X^3 and X^4 is $-NR^{13}-$, and the $-NR^{13}-$ is $-NR^a-$ (R^a represents an acyl group derived from sulfonic acid) and the other is an oxygen atom, $-NR^{13}-$ (R^{13} represents a hydrogen atom, a hydrocarbon group optionally having a substituent or an acyl group optionally having a substituent), a sulfur atom or $-CR^{15}R^{16}-$).

[Claim 9]

The phosphoric acid derivative according to claim 8, wherein the phosphoric acid derivative represented by the general formula (1a) is an optically active phosphoric acid derivative.

[Claim 10]

The phosphoric acid derivative represented by the general formula (1b):



(1b)

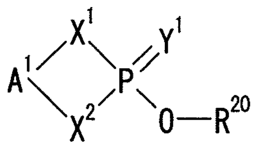
(wherein A^2 represents a spacer, and R^{21} to R^{24} each independently represent a hydrocarbon group optionally having a substituent or a hetrocyclic group optionally having a substituent).

[Claim 11]

The phosphoric acid derivative according to claim 10 wherein the phosphoric acid derivative represented by the general formula (1b) is an optically active phosphoric acid derivative.

[Claim 12]

A phosphoric acid derivative represented by the general formula (9):



(9)

(wherein A^1 represents a spacer; X^1 and X^2 each independently represent a divalent nonmetal atom or a divalent nonmetal atomic

group; Y^1 represents an oxygen atom or a sulfur atom; and R^{20} represents an allyl group optionally having a substituent or a benzyl group optionally having a substituent).

[Document Name] Abstract

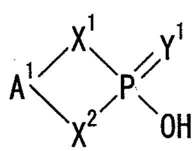
[Abstract]

[Problem to be solved]

The present invention was done in view of the aforementioned problems, and an object of the present invention is to provide a process of production of amines useful as an intermediate or the like for drugs, agricultural chemicals or the like, particularly, optically active amines in a good yield and a high optical purity without extra post-treatment or the like, and a phosphoric acid derivative, particularly, an optically active phosphoric acid derivative useful for production of the amines or the like.

[Means for solving the problems]

A process for preparing an amine, comprising reacting an imine compound and a nucleophilic compound (provided that trialkylsilyl vinyl ethers are excluded) in the presence of a phosphoric acid derivative represented by the general formula (1):



(1)

(wherein A^1 represents a spacer; X^1 and X^2 each independently represent a divalent nonmetal atom or a divalent nonmetal atomic group; and Y^1 represents an oxygen atom or a sulfur atom).